AMBOSS USMLE STEP 2

Cardiology – Educational Objectives (258)

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- **Dr Mohammed Zaki**
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Atrial fibrillation

Nondihydropyridine calcium channel blockers such as verapamil are a first-line option for ventricular rate control in patients with stable Afib. This patient's normal TSH, electrolyte, and troponin levels rule out reversible or treatable causes of Afib. Since this patient is symptomatic with intermittent palpitations and tachycardia, the next appropriate step is rate control. The target resting heart rate for patients with Afib is < 110/min for asymptomatic patients and < 80/min for symptomatic patients. Furthermore, the need for anticoagulation should be evaluated in all patients with Afib. Cardioversion can be considered as an alternative to rate control, but this procedure carries a high risk of thromboembolism. Therefore, patients like this one who have been in Afib for > 48 hours should receive prophylactic anticoagulation therapy for 3 weeks before cardioversion. This period can be shortened if atrial thrombi are excluded by transesophageal echocardiography.

This patient initially presented with what was presumed to be new-onset symptomatic Afib. While controlling rate and/or rhythm, as well as providing anticoagulation (according to CHA2DS2-VASc score), are the key therapeutic principles in this condition, the patient's spontaneous conversion to sinus rhythm and her CHA2DS2-VASc score of 1 indicate that no further management (i.e., medical or electrophysiological intervention), aside from observation, is necessary at this time. Nonetheless, underlying causes of Afib (such as structural heart disease, hyperthyroidism, electrolyte imbalances) should be investigated.

Afib can lead to stasis of blood and thrombi formation in the atrium, which, in patients undergoing cardioversion, can get dislodged and cause thromboembolism. Therefore, anticoagulation with a direct oral anticoagulant (DOAC) such as apixaban should be initiated prior to cardioversion and continued for ≥ 4 weeks after the procedure in patients with Afib starting in the past 48 hours who have a moderate to high thromboembolic risk, such as this patient. If DOACs are contraindicated, heparin (e.g., for pregnant patients) or warfarin (e.g., for patients with mechanical heart valves) can be used. In patients with new-onset Afib for > 48 hours or if the duration is unknown, anticoagulation should be given for at least 3 weeks before cardioversion and the need for rate control should be evaluated. The time to cardioversion can be shortened by performing transesophageal echocardiography after therapeutic anticoagulation, as this procedure detects atrial thrombi with greater sensitivity than transthoracic echocardiography.

Atrial flutter most commonly develops as a result of a macroreentrant circuit within the right atria that travels along the tricuspid annulus and passes through the cavotricuspid isthmus. Although the exact etiology remains unclear, a number of risk factors such as hypertension and obesity are known to contribute. Most patients with atrial flutter are asymptomatic, but symptoms of arrhythmia such as palpitations, lightheadedness, syncope, and dyspnea can also develop. The ECG typically shows a regular rhythm, sawtooth P waves, and possibly a concomitant atrioventricular block with a fixed pattern (2:1 in this case). Stable patients who do not convert spontaneously to sinus rhythm should usually undergo pharmacological or electrical cardioversion. A common complication of atrial flutter is progression to atrial fibrillation. Because the risk of thromboembolism in atrial flutter is similarly elevated as in atrial fibrillation, the indications for anticoagulation are the same.

Atrial fibrillation (Afib) is a supraventricular tachyarrhythmia caused by uncoordinated atrial activation. Although usually asymptomatic, it can also cause symptoms such as this patient's dizziness and palpitations. In particular, acute alcohol consumption often triggers paroxysmal Afib (also known as “holiday heart syndrome”), which subsides within 7 days without intervention. To prevent similar episodes, this patient should abstain from alcohol in the future.

Unstable Afib, as seen in this patient, should be managed with immediate electrical synchronized cardioversion. Older patients with underlying heart disease (such as this 63-year-old man with coronary artery disease) are at increased risk of hemodynamic compromise. Signs of hemodynamic instability include hypotension, confusion, symptoms of heart failure (e.g., dyspnea), and chest pain. The goal of synchronized cardioversion is to terminate Afib and thereby restore hemodynamic stability as well as prevent further progression to ventricular tachycardia or ventricular fibrillation. Synchronized cardioversion can also be considered for hemodynamically stable patients with acute onset of Afib (within the past 48 hours).

Rhythm control with cardioversion is a treatment approach used for some patients with new-onset Afib (e.g., young and/or pregnant patients) and aims to restore sinus rhythm in order to prevent atrial remodeling and improve symptoms. However, prolonged episodes of Afib significantly increase the risk of atrial thrombi formation and subsequent dislodgement during cardioversion. Therefore, hemodynamically stable patients who have had Afib for ≥ 48 hours or an unknown period of time require systemic anticoagulation for 3 weeks prior to cardioversion. If cardioversion is desired earlier (e.g., in pregnant and/or symptomatic patients), the time to cardioversion can be shortened by performing transesophageal echocardiography (TEE) to detect potential thrombi and guide further management.

TEE is not required prior to cardioversion in hemodynamically unstable patients with Afib, as the risk of complications from hemodynamic instability outweighs the risk of thromboembolic complications after cardioversion. The management of hemodynamically stable, symptomatic patients with Afib with rapid ventricular response usually also includes rate control (e.g., with a beta blocker) as one of the first steps in management. Although this patient may be considered for rate control, TEE is the most appropriate answer given the options provided in this question.

Inhibition of the synthesis of vitamin K-dependent factors by warfarin is used in women with Afib and a CHA2DS2-VASc score ≥ 3 to prevent atrial thrombus formation and subsequent thromboembolic events (e.g., acute limb ischemia, stroke). This patient's CHA2DS2-VASc score is 4 (history of HTN, history of diabetes, age 65–74, female).

Absent P waves and irregularly irregular RR intervals on electrocardiogram would be consistent with atrial fibrillation (Afib) a significant risk factor for atrial thrombus formation due to the rapid, irregular contraction of the atria and subsequent blood stasis. Thrombi formed in the left atrium or left ventricle can fragment into emboli and disperse into the arterial circulation, leading to ischemic events. This patient has multiple risk factors for Afib, including her age, hypertension, and diabetes.

All patients with new-onset symptomatic Afib should be evaluated for potential causes of arrhythmia. Measurement of serum TSH levels is the best initial step in the diagnosis of hyperthyroidism, a common cause of symptomatic Afib that can manifest with hypertension with wide pulse pressure (140/70 mm Hg), tremor, and warm skin. Individuals with Graves disease, the most common cause of hyperthyroidism, can also develop pretibial myxedema, which manifests as nonpitting bilateral pretibial edema. Given that this patient has classic features of hyperthyroidism and Graves disease, her TSH levels should be measured at this time. Treatment of hyperthyroidism (e.g., with antithyroid drugs and/or surgery) in patients who have developed Afib usually results in conversion to sinus rhythm. Beta-blockers such as propranolol can be administered to reduce the heart rate and provide symptomatic relief. Electrical or pharmacological cardioversion is a last-resort treatment in patients who still have Afib after achieving euthyroid status.

Automatic depolarizing foci near the pulmonary vein are typically involved in the pathogenesis of atrial fibrillation. Ablation of atrial tissue around the pulmonary veins (pulmonary vein isolation) would prevent these depolarizing foci from spreading to the rest of the myocardium.

Aortic Stenosis

This patient has aortic stenosis (AS), most likely secondary to calcification and fibrosis of the aortic valve, which becomes more prevalent with older age. The increased afterload created by the stenotic aortic valve reduces cardiac output, which results in angina, syncope, and ultimately, heart failure. Other common underlying risk factors for AS, especially in younger patients, include bicuspid aortic valves and a history of rheumatic fever. To confirm this patient's diagnosis and evaluate the extent of AS, the next best diagnostic step would be to perform transthoracic echocardiography.

This patient's auscultation findings are consistent with aortic stenosis, which causes left ventricular outflow obstruction. The result is dizziness and exacerbation of dyspnea upon exertion, and weak peripheral pulses (pulsus parvus et tardus). Incomplete left ventricular emptying may also cause pulmonary venous congestion, which further exacerbates dyspnea.

Dyspnea is an early sign of heart failure, which occurs in severe AS as a result of left ventricular diastolic dysfunction. While patients with AS can be asymptomatic for years, the onset of symptoms usually indicates a progression to severe AS. Mortality rates increase from less than 1% per year in asymptomatic patients to over 50% within the first two years after the onset of symptoms if left untreated. Dyspnea is the strongest predictor of a poor prognosis, followed by syncope and angina pectoris. Approximately half of AS patients with dyspnea die within 2 years of symptom onset. Aortic valve replacement can slow the rapid decline in life expectancy after the onset of symptoms.

In AS, blood flow from the left ventricle to the aorta is obstructed by the narrowed aortic valve opening (increased afterload), which, over time, results in left ventricular hypertrophy (LVH). LVH leads to increased left ventricular oxygen demand, resulting in myocardial ischemia (angina) during periods of strenuous exercise or stress. The inability to maintain cardiac output during exertion causes transient cerebral hypoperfusion and, therefore, presyncope or syncope. The presence of symptoms in patients with AS is an indication for surgical repair, as symptomatic AS carries a poor prognosis.

Transthoracic echocardiography is the best confirmatory test in patients with suspected aortic stenosis (AS), the most likely cause of this patient's syncope. In early stages of AS, patients are typically asymptomatic at rest. However, during exertion, peripheral vasodilation occurs to increase blood flow to muscles. If stenosis at the aortic valve is severe enough, it obstructs blood flow, thereby preventing an increase in cardiac output to maintain blood pressure during exertion, which leads to hypotension, decreased cerebral blood flow, syncope, dizziness, dyspnea, and angina pectoris. A delayed pulse supports this diagnosis. Cardiac auscultation typically shows a crescendo-decrescendo systolic murmur.

Aortic Dissection

Contrast-enhanced CT angiography (CTA) is the definitive diagnostic test of choice for aortic dissection in hemodynamically stable patients because of its high sensitivity and specificity, the speed and ease with which it can be conducted, and its widespread availability. A false lumen detected on imaging is consistent with aortic dissection. Further, nonspecific findings of aortic dissection in this patient include an elevated D-dimer level due to clot formation in the lumen and pleural effusion on chest x-ray. In this woman, CTA can also be used to rule out pulmonary embolism (which can lead to nonspecific symptoms and a high D-dimer level) and acute aortic occlusion (which can cause leg paresthesia and decreased femoral pulse). For hemodynamically unstable patients or patients with contraindications to contrast agents (e.g., renal insufficiency), transesophageal echocardiography should be performed instead of CTA.

Hypertension is the strongest risk factor for aortic dissection; approx. 70% of patients with aortic dissection have elevated blood pressure. Hypertension leads to shear stress and weakening of the vascular wall, which increases the risk of tearing of the tunica intima and consequent formation of a false lumen in the intima-media space. Blood pressure control is essential in all patients to prevent further progression of the dissection. Stanford A dissection, which this patient most likely has, requires immediate surgery, while Stanford B dissection can often be treated conservatively in hemodynamically stable patients unless complications such as rupture or occlusion occur.

Muffled heart sounds are a sign of cardiac tamponade, a possible complication of ascending aortic dissection (Stanford type A) due to progression of the dissection beyond the aortic root. If the dissection results in a tear of the tunica externa, aortic blood can leak into the pericardium. Pericardial fluid will decrease the transmission of heart sounds to the precordium. Other possible complications of ascending aortic dissections include myocardial infarction (due to coronary artery occlusion), aortic regurgitation (extension of the dissection into the aortic valve), and stroke (extension of the dissection into the carotids).

Emergency open aortic repair surgery with graft placement is critical in the management of ascending aortic dissections (Stanford type A) because of the high risk of complications such as aortic rupture, acute aortic regurgitation, myocardial infarction, and cardiac tamponade. Simultaneously to surgery, this patient requires management of hypotensive shock with IV fluids and, if necessary, vasopressors, as well as supportive care for pain and anxiety. Patients with uncomplicated dissections of the descending aorta (Stanford type B) can be treated conservatively with observation, blood pressure control, and analgesia unless complications develop (e.g., aortic rupture, renal failure, abdominal pain due to intestinal ischemia). Elevated troponin I and lactate dehydrogenase levels indicate myocardial stress due to involvement of the coronary arteries, while D-dimer levels are commonly elevated in aortic dissection and may have prognostic value.

Aortic dissection typically occurs in males 60–80 years of age with hypertension. It causes sudden severe pain, typically of the anterior chest (in an ascending dissection) or the back and interscapular region (in a descending dissection), which can migrate as the dissection progresses. Other clinical features include elevated blood pressure, asymmetrical blood pressure and pulse readings between limbs, diminished distal pulses, syncope, sweating, and confusion. Aortic dissection manifests as a widened mediastinum on chest x-ray. Extension of the dissection into the aortic valve causes aortic regurgitation. However, unlike the murmur of aortic regurgitation from aortic valve disease, which is prominent along the left sternal border, the murmur of aortic regurgitation from aortic dissection is prominent along the right sternal border.

Conservative therapy with observation, blood pressure control, and analgesia is appropriate for most patients with uncomplicated descending aortic dissections (Stanford type B). Blood pressure control is essential in all patients with aortic dissection to prevent further progression of the dissection. Intravenous beta blockers (e.g., labetalol, esmolol) lower the heart rate and reduce the left ventricular ejection fraction, thereby reducing shearing forces within the aorta. If IV beta blocker therapy does not lower systolic blood pressure to 90–120 mm Hg, patients should also receive vasodilators (e.g., sodium nitroprusside). To avoid reflex tachycardia, beta-blocker therapy should be started before vasodilators. Patients with uncomplicated type B dissections do not require surgical intervention unless they develop complications (e.g., aortic rupture, renal failure, abdominal pain due to intestinal ischemia). Patients treated conservatively who develop worsening pain or features suggestive of complications should have vascular imaging repeated immediately.

Transesophageal echocardiography (TEE) is a fast, portable test with high sensitivity and specificity for aortic dissection. TEE is the preferred initial study in hemodynamically unstable patients (it can be rapidly performed at the bedside or in the operating room) and patients with renal insufficiency (because of the increased risk of developing contrast-induced nephropathy with CT angiography) or contrast allergy. This imaging modality helps visualize intimal dissection flaps, true and false lumens, thromboses in false lumen, aortic regurgitation, and pericardial effusion, and it aids in determining whether surgical intervention is warranted. TEE cannot be used to assess dissections below the diaphragm; in such cases, CT angiography is preferred.

Acute aortic occlusion (AAO) is a life-threatening vascular event with clinical findings that vary depending on the location of the occlusion. These findings may include symptoms of lower limb and mesenteric ischemia, as seen in this patient. Causes of AAO include atherothrombosis, occlusion of a stent or vascular graft, aortic dissection, and aortic embolism. Aortic emboli that are large enough to lead to AAO typically have a cardiac origin and develop as a result of incomplete atrial/ventricular emptying in cardiac arrhythmias (e.g., atrial fibrillation), valvular heart disease (e.g., mitral stenosis), or conditions that lead to blood pooling, such as left ventricular aneurysm and pseudoaneurysms (e.g., following recent anterior MI). In this patient with atriomegaly and an irregular pulse suggestive of atrial fibrillation, thromboembolism is the most likely cause of AAO.

This patient presents with cardiac auscultation findings characteristic of mitral stenosis (apical opening snap followed by a diastolic murmur). In combination with atriomegaly on echocardiography and a childhood history of arthritis and angina pectoris, the mitral stenosis in this patient most likely developed as a result of chronic rheumatic heart disease. This condition is a complication of untreated group A streptococcal infection and is more common in areas where access to antibiotics is limited.

Aortic aneurysm - Abdominal

Elective surgical repair is indicated for large asymptomatic AAAs (≥ 5.5 cm in men; ≥ 5.0 cm in women), rapidly expanding AAAs (≥ 0.5 cm/6 months), saccular aneurysms, and/or symptomatic AAAs (as these are most likely to rupture) regardless of size. This patient has a saccular AAA that has rapidly grown over the past year and therefore requires surgery. Endovascular aneurysm repair is recommended for AAA in patients with suitable anatomy because it is minimally invasive and can be performed under local anesthesia. Furthermore, this approach is preferred in individuals with high operative risk, such as this patient with multiple comorbidities.

This patient most likely has a ruptured abdominal aortic aneurysm (AAA). The pathophysiology of AAA is not fully understood, but numerous genetic and environmental factors, such as smoking, are believed to cause inflammation and proteolysis of connective tissue within the aortic wall. This leads to loss of structural integrity and weakening of the aorta. Other risk factors for AAA include advanced age and male sex. When high aortic wall stress is applied, as in hypertension, further weakening, widening, and rupture of the aortic wall can occur. AAAs are most commonly located below the renal arteries (infrarenal).

Open emergency surgery is the most appropriate next step for this patient who most likely has an AAA rupture. The findings of hypotension, tachycardia, and tachypnea indicate that this patient is in severe hemorrhagic shock. In a hemodynamically unstable patient with a high clinical suspicion for ruptured AAA, treatment should not be delayed for any confirmatory imaging. An alternative to open surgery is endovascular aneurysm repair, which is recommended over open surgery in current guidelines if it is anatomically feasible. Without immediate repair, AAA rupture is usually fatal within hours.

A history of smoking is the strongest independent risk factor for the development and growth of an AAA. The risk of a clinically detectable aneurysm, as seen in this patient with 60 pack-years of smoking, may be up to 25 times greater than in a man the same age who has never smoked. Because smoking increases the risk of AAA so dramatically, the US Preventive Services Task Force recommends a single screening ultrasound for all males with a history of smoking between the ages of 65 and 75. Refraining from or quitting smoking is also the single most important measure for preventing AAA. Risk factors for AAA rupture include a large aneurysm diameter (> 5.5 cm), rapid expansion rate (> 1 cm/year), and smoking.

Patients with a suspected asymptomatic AAA should undergo abdominal ultrasonography to confirm the diagnosis (dilatation of the aorta ≥ 3 cm) and evaluate the extent of disease, including location and size of the aneurysm, presence of a blood clot, and presence of comorbid iliac artery aneurysms. The sensitivity and specificity of abdominal ultrasonography for AAA are nearly 100%. After the diagnosis is established, management strategies depend on the risk factors for rupture (e.g., aneurysm diameter and rate of expansion).

Aortic aneurysm - Thoracic

Cystic medial necrosis of the aorta can lead to the development of an ascending thoracic aortic aneurysm (TAA), which may manifest with back pain and chest pressure. Different conditions can be associated with the occurrence of TAAs of the ascending aorta. A patient presenting with signs of a TAA and a tall height (194 cm) may have Marfan syndrome. Other conditions associated with TAA include Ehlers-Danlos syndrome, hypertension, the occurrence of a congenital bicuspid aortic valve, and cardiovascular syphilis causing aortitis.

A CT angiography (CTA) of the chest is the preferred imaging modality for investigating mediastinal abnormalities detected on chest x-ray (e.g., mediastinal widening or a mediastinal mass) as it is accurate, rapid, and non-invasive. This patient's x-ray findings are strongly suggestive of a TAA, which can manifest with chest discomfort and cough due to compression of the tracheobronchial tree (although most TAAs are asymptomatic, and this patient's cough may be a sequela of his recent upper respiratory tract infection). However, a chest x-ray cannot accurately determine the underlying cause of mediastinal widening. CTA is the best confirmatory test for TAAs, delineates the size and length of the TAA, and detects complications (e.g., thrombus formation, free/contained TAA rupture), thereby providing valuable information for planning management. MR angiography is a reasonable alternative to CTA in hemodynamically stable patients who should avoid ionizing radiation.

Acute limb ischemia

Digital subtraction angiogram (DSA) is an imaging modality used to diagnose ALI. In patients with ALI, diagnostic evaluation should only be performed if treatment can be delayed without posing a threat to the extremity. DSA is useful for identifying arterial occlusions or dissections as an underlying etiology of ALI and facilitates immediate therapeutic intervention, e.g., catheter-directed thrombolysis.

This patient presents with limb-threatening ischemia (Rutherford stage IIb), indicated by his severe pain, decreased motor function and sensation, and inaudible arterial Doppler signal. In addition to intravenous heparin therapy (to prevent further clot formation and embolization), the patient requires revascularization within 6 hours to restore blood flow and increase the probability of limb salvage. Balloon thrombectomy and bypass surgery are appropriate revascularization procedures for patients with embolic acute limb ischemia and a threatened extremity.

The persistent vasoplegia associated with septic shock frequently requires prolonged treatment with vasopressors to maintain a mean arterial blood pressure > 65 mm Hg. Norepinephrine is a vasopressor that preferentially agonizes alpha-1 receptors, causing vasoconstriction and an increase in systemic vascular resistance. Prolonged alpha receptor agonism can cause distal arterioles and their branches (especially cutaneous branches) to constrict to the point of causing distal ischemia and consequent necrosis. This phenomenon is most commonly observed in the fingertips and distal toes and manifests with symmetrical discoloration and coldness.

Echocardiography can be used to visualize an atrial thrombus, which can develop as a complication of atrial fibrillation (Afib). This patient's irregular pulse is suggestive of Afib. The atrial thrombus (or parts of it) may dislodge and embolize into the systemic circulation, thereby leading to arterial occlusion and subsequent ischemia. The most common location of arterial occlusion due to arterial embolism is the femoropopliteal artery. ALI is commonly caused by thrombosis secondary to peripheral artery disease (PAD); however, the absence of preexisting claudication in this case makes PAD a less likely diagnosis.

Sudden onset of ALI in a previously asymptomatic patient (no trauma and no features of peripheral artery disease such as claudication) is most likely caused by arterial embolism. Arterial embolisms most commonly originate from a cardiac thrombus, which typically forms if there is intracardiac blood stasis (e.g., due to atrial fibrillation or complications of myocardial infarction such as noncontractile myocardium or ventricular aneurysm). This patient's sensory loss and muscle weakness strongly suggest that the right limb is under immediate threat. Management of ALI in a viable or threatened limb begins with an IV heparin bolus followed by continuous infusion and emergent revascularization (via catheter-directed thrombolysis, percutaneous mechanical thromboembolectomy, or open thromboembolectomy) to restore blood flow to the extremity.

ALI most commonly results from the rupture of an atherosclerotic plaque or thrombosis in a previously stenotic but patent artery, such as those in patients with PAD. In PAD, collateral circulation often gradually develops, which protects against sudden, severe ischemia. Therefore, in patients with PAD, the manifestation of ALI is typically less severe than arterial embolism and symptoms usually develop within a few hours to a few days (i.e., acute-on-chronic limb ischemia)

Angioedema

C1 inhibitor deficiency is the underlying cause of HAE. A deficiency or dysfunction of C1 inhibitor results in elevated levels of bradykinin, which is a strong vasodilator. HAE is characterized by recurrent episodes of swelling without hives or pruritus that primarily affects the skin and mucosa of the gastrointestinal and upper respiratory tracts. The most common triggers are stress and trauma, especially from dental procedures. The episodes are usually self-limited and resolve within 2–4 days. HAE is an autosomal dominant disorder, however, about 25% of cases are due to spontaneous mutations.

Aneurysm

A femoral artery pseudoaneurysm occurs in ~ 1% of patients following iatrogenic femoral artery puncture (e.g., percutaneous cardiac catheterization via the femoral artery). Femoral artery pseudoaneurysms manifest with pain in the groin, a pulsatile mass, and a systolic bruit over the swelling. Duplex ultrasonography is required to distinguish a femoral artery pseudoaneurysm from other conditions that may manifest similarly (e.g., femoral artery hematoma, femoral arteriovenous fistula, femoral artery aneurysm, saphenous varix). On ultrasound, a femoral artery pseudoaneurysm is usually visible as a nonhomogenous hypoechoic mass that is connected to a femoral vessel via a patent track. Bidirectional flow through the neck of the aneurysm may also be seen.

A palpable pulsatile mass in the thigh with a bruit on auscultation is characteristic of an unruptured femoral artery aneurysm. This condition can be asymptomatic or manifest with thigh or groin pain and is often diagnosed incidentally during the workup of other aneurysms or vascular conditions. Risk factors for femoral artery aneurysms include ASCVD risk factors (e.g., hypertension, hypercholesterolemia, smoking).

Ultrasound-guided thrombin injection into the pseudoaneurysm sac initiates the rapid formation of a fibrin clot, stopping blood flow to the hematoma. This procedure has become the gold standard for the treatment of uncomplicated postcatheterization pseudoaneurysms that measure ≥ 3 cm, and it has a success rate of > 90%.
Pseudoaneurysms are most often iatrogenic (e.g., a complication of vascular puncture or cardiovascular surgery) and typically manifest within 24 hours following the procedure. In some cases, iatrogenic pseudoaneurysms only become symptomatic 7–10 days after the intervention. The incidence of iatrogenic pseudoaneurysms is low: they are reported following < 1% of all diagnostic and therapeutic catheterizations.
In contrast, true aneurysms of the femoral artery usually require open surgical repair if they become symptomatic or measure ≥ 3 cm.

Atrioventricular block

Mobitz type II AV block is an unstable bradyarrhythmia that requires immediate treatment because it can progress to third-degree heart block and death. The first step in management is to determine hemodynamic status. Unstable patients require immediate treatment with transcutaneous (or transvenous) cardiac pacing. Placing a transcutaneous pacemaker is only a temporary measure until the patient is hemodynamically stable and can be further evaluated and treated for reversible causes of AV block. In patients with no reversible causes, definitive treatment includes placement of a permanent pacemaker to bypass the AV nodal block. In addition to temporary cardiac pacing, prompt treatment with atropine and beta-adrenergic agents (e.g., dopamine, dobutamine, epinephrine) may be indicated. Administration of IV atropine is the first-line treatment for most cases of symptomatic bradycardia. However, in patients with an infranodal block, such as Mobitz type II AV block, atropine is often ineffective and may in rare cases worsen the symptoms.

Transcutaneous (or transvenous) cardiac pacing is indicated in patients with symptomatic high-risk AV blocks (e.g., Mobitz type II block or third-degree block). Transcutaneous pacing is only a temporary measure. Once the patient is stabilized, the cause of the third-degree AV block should be investigated, followed by a long-term solution (e.g., permanent cardiac pacing) if no reversible cause is found. This patient's third-degree AV block is likely an adverse effect of her medication (a beta blocker) and may be reversed with drug discontinuation.

This patient's dyspnea, dizziness, syncopal episodes (Stokes-Adams attacks), bradycardia, recent inferior myocardial infarction (MI), and ECG findings are consistent with a third-degree atrioventricular block (i.e., complete AV block). This condition is characterized by AV dissociation, in which the atria (P waves) and the ventricles (QRS complexes) beat independently of one another. Third-degree AV blocks occur due to impaired conduction at the level of the AV node (~ 20%), bundle of His, or below the His bundle (most common; ~ 60%). A block above the His bundle is associated with narrow QRS complexes (< 120 ms), while a block below the His bundle is characterized by wide QRS complexes. Additionally, the atrial rate is greater than the ventricular rate (i.e., more P waves than QRS complexes) and both atrial and ventricular rates are constant.

Third-degree AV block may complicate an inferior MI (because the AV node and His bundle are primarily supplied by the right coronary artery) or an anterior MI (because the His bundle may receive blood from the septal branches of the left coronary artery). Other causes of third-degree AV block include infections (e.g., Lyme disease, bacterial endocarditis), cardiomyopathy, hyperkalemia, and iatrogenic effects (e.g., cardiac interventions, drugs such as beta-blockers).

Aortic regurgitation

A water hammer pulse is a classic finding on cardiovascular examination in patients with AR. On palpation of a peripheral artery, such as the radial artery, the clinician will feel rapid engorgement of the artery followed by a significant, prompt collapse of the vessel. This is due to the incompetent aortic valve failing to maintain adequate diastolic pressure in the arterial system, which also causes a widened pulse pressure. Other findings of AR include pulse synchronous head nodding (de Musset's sign) and, occasionally, a rumbling, low-pitched mid-diastolic murmur (Austin Flint murmur) that is caused by the regurgitant blood striking the anterior leaflet of the mitral valve, leading to premature closure of the mitral leaflets. Patients with Marfan syndrome often have aortic disease (e.g., aortic regurgitation) as a consequence of cystic medial degeneration.

An early diastolic decrescendo murmur that is heard best at the left sternal border suggests aortic regurgitation (AR). Regurgitation of blood from the aorta into the left ventricle (LV) causes widened pulse pressure with a decreased diastolic blood pressure. To maintain an adequate cardiac output despite regurgitation, initially, there is a compensatory increase in stroke volume. Over time, the increased LV end-diastolic volume leads to LV enlargement and eccentric myocardial hypertrophy. Patients may be asymptomatic for decades despite progressive LV dilation. In chronic AR, this compensatory response results in left ventricular dysfunction, and patients develop signs and symptoms of left heart failure (exertional and nocturnal dyspnea, S3 gallop). The diagnosis of AR should be confirmed with transthoracic echocardiography. Maneuvers that increase afterload (e.g., handgrip) increase the intensity of the associated murmur as a result of the enlargement of regurgitation volume across the valve.

The patient has a diastolic murmur, which shortens the list of differentials here to mitral stenosis (MS), aortic regurgitation (AR), tricuspid stenosis (TS), and pulmonary regurgitation (PR). Let's have a look at the location of the murmur: it is best heard at the left sternal border near Erb point (cardiology). This location makes MS unlikely (usually best heard at the apex) but is consistent with a murmur caused by AR due to valvular disease. Now, here comes the tricky part. In this patient, TS and PR cannot be excluded by cardiac auscultation because the left sternal border is also the location at which murmurs due to TS and PR are best heard. However, subtle details make AR more likely. PR can occur in patients with pulmonary hypertension due to lung disease (cor pulmonale) or chronic congestive heart failure, but this patient has no clinical features to suggest either of these etiologies. Isolated TS or PR are extremely rare (usually caused by endocarditis in intravenous drug users, or by congenital heart defects), and manifest with features of right heart failure, which are not seen here. This patient's history of emigration from Nepal increases the likelihood that the underlying etiology of valvular heart disease is rheumatic heart disease, which most commonly affects the mitral and aortic valves. In patients with AR, a widened pulse pressure (due to increased end-diastolic volume and a subsequent increase in stroke volume) is a common finding. Other common causes of AR include a congenital bicuspid aortic valve (most common cause of AR in high-income countries) and aortic root dilation due to connective tissue disorders (e.g., Marfan syndrome, Ehlers-Danlos syndrome). In contrast to AR due to valvular disease, the murmur of AR secondary to aortic root diseases is heard best over the right upper sternal border. Timing the murmur against the carotid pulse is an important skill to master; if you are finding it difficult to time the murmur, try listening to the murmur again between 10 and 20 seconds using a slow playback speed and gradually increase the playback speed until you are proficient in timing the murmur.

Congenital bicuspid aortic valve (BAV) is the most common cause of AR in young adults in high-income countries. Patients with congenital BAV can present with features of aortic stenosis and/or features of regurgitation. The clinical manifestations of congenital BAV vary depending on the presence of associated abnormalities (e.g., aortic root dilation) and left ventricular function. Aortic regurgitation often occurs due to underlying leaflet abnormalities (e.g., prolapse) and/or valvular apparatus dilation.

Acute coronary syndrome

Emergency revascularization is the most important step in the management of patients with acute STEMI because it restores the patency of the occluded coronary artery, limiting a further increase in the size of the infarction. Percutaneous transluminal coronary angioplasty (PCTA) is the preferred method of revascularization. Since early reperfusion is associated with improved clinical outcomes, door-to-balloon time should be < 90 minutes. Fibrinolytic therapy may be considered if PCTA fails or cannot be performed within 120 minutes of the patient arriving at the hospital. Oral dual antiplatelet therapy (P2Y12 receptor inhibitor and aspirin) and intravenous anticoagulation therapy (heparin or bivalirudin) are also indicated for patients with STEMI and may be initiated during or prior to transportation to the cardiac catheterization laboratory, but definitive treatment should not be delayed. Beta-blocker therapy is associated with improved outcomes for patients and must be initiated within the first 24 hours of admission unless there are contraindications. Patients should also be started on high-intensity statin therapy regardless of baseline cholesterol levels.

Intravenous fluids (usually normal saline) should be administered in hemodynamically unstable patients with right ventricular infarction to optimize preload. Maintaining preload is critical because right ventricular ischemia impairs left ventricular filling in two ways: (1) it impairs right ventricular contraction, which decreases the volume delivered to the left ventricle, and (2) it reduces right ventricular relaxation, which increases the right ventricular diastolic pressure and decreases the volume of the left ventricle by pushing the septum into the left ventricle. Increasing the preload optimizes left ventricular filling and reduces hemodynamic instability. If blood pressure cannot be maintained with a fluid bolus, vasopressors and/or an intra-aortic balloon pump can be used.

An ECG and troponin test should be ordered to evaluate for acute coronary syndrome (ACS). This patient's acute chest pain, shortness of breath, diaphoresis, and nausea should raise suspicion for an MI. She has many risk factors for perioperative ACS, including a history of coronary artery disease, hypertension, diabetes mellitus, and a 12 pack-year smoking history. The patient's history of ischemic heart disease and insulin-dependent diabetes entails a ~ 6.6% perioperative risk of a major cardiac event, based on the revised cardiac risk index.

An atrial gallop (S4) results from atrial contraction against a stiff ventricle. It is frequently heard in the acute phase of an MI because of impaired relaxation of the ischemic left ventricle. An S4 may also be heard in conditions that cause ventricular hypertrophy, such as hypertrophic cardiomyopathy, aortic stenosis, or hypertension. Older patients can have an S4 as a normal finding because ventricular compliance decreases with age.

A ventricular gallop (S3), on the other hand, is caused by a sudden deceleration of blood flow from the left atrium into the left ventricle during early diastole. This finding can be normal in young adults (< 40 years) or pregnant women, but it is abnormal in older adults. An S3 may be heard in dilated cardiomyopathy, heart failure, or valvular diseases such as chronic mitral or aortic regurgitation. It is not a common finding in acute M

Angina or angina equivalents (e.g., diaphoresis, nausea) that are of new-onset, present at rest, and persistent, worsening, or changing in character should raise suspicion for acute coronary syndrome (ACS). The three forms of ACS are ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and unstable angina (UA). In UA, the ECG is normal or discloses nonspecific findings (e.g., ST depression, T-wave inversion, poor R wave progression) and serum troponin studies are normal. Patients with UA are managed with the same measures used in other forms of ACS, i.e., anticoagulant, antiplatelet, beta blocker, statin, ACE inhibitor, and analgesic therapy, and cardiac catheterization for coronary angiography and revascularization. NSTEMI or STEMI within the past 2 days and ongoing unstable angina are absolute contraindications to cardiac stress testing. Fibrinolytic therapy is not indicated for NSTEMI or UA.

Amiodarone

The risk of developing chronic interstitial pneumonitis correlates with the total cumulative dose of amiodarone. Symptoms may develop 6 to 12 months after initiation and include insidious onset of nonproductive cough, dyspnea, weight loss, and fatigue. Lung auscultation usually reveals bilateral dry crackles during inspiration. Chest radiograph typically shows ground-glass opacifications.

Patients with preexisting lung disease are at particularly high risk of developing this complication, and this should be considered before starting this medication.

Blunt trauma

Blunt force aortic injuries range from small intimal tears and intramural hematomas to aortic rupture. Contrast-enhanced CT angiography (CECT angiography) is indicated for the diagnosis of aortic injury in hemodynamically stable patients and should be performed if the patient has symptoms suggestive of aortic injury (e.g., chest pain), a history of high-energy trauma, or features that suggest aortic injury on the FAST scan (e.g., hemothorax) or chest x-ray (e.g., mediastinal widening, aortic knob loss). CECT angiography has high sensitivity and specificity, can screen for additional vascular injuries (e.g., abdominal aortic injury), and provides anatomical information for planning surgical management. Patients who are hemodynamically unstable should be urgently evaluated with transesophageal echocardiography in the operating room.

A widened mediastinum, esophageal deviation, depression of the left main bronchus, and hemothorax (suggested by left pleural effusion) are consistent with thoracic aortic rupture (TAR). TAR can be traumatic (e.g., due to high-velocity blunt chest wall trauma) or spontaneous (e.g., following aortic dissection). Only around 20% of patients with blunt traumatic aortic injuries survive long enough to reach the hospital; therefore, immediate resuscitation and prompt surgical repair of the thoracic aorta is required in patients with suggestive findings (e.g., symptoms of respiratory distress, features of hemorrhagic shock).

In the context of a serious motor vehicle collision, this patient's hypotension and tachycardia refractive to fluid resuscitation, including vasopressors, combined with atrial fibrillation on ECG and a negative FAST, are highly suspicious for cardiac contusion. Cardiac contusions may manifest with clinical features ranging from asymptomatic arrhythmias to rapidly fatal cardiac rupture. Blunt chest trauma and/or sudden deceleration can lead to decreased contractility and arrhythmias due to injury to cardiac myocytes and pacemaker cells. Decreased contractility directly contributes to cardiogenic shock with decreased cardiac output and hypotension, as in this patient.

Bradycardia

Atropine is an anticholinergic agent that is used to increase heart rate. Intravenous atropine is the first-line treatment in patients who present with unstable bradycardia. Asymptomatic patients do not require treatment.

Coronary artery disease

Atenolol is a β1-selective adrenergic receptor blocker used as first-line therapy to improve exercise tolerance and reduce the frequency of anginal episodes in patients with stable CAD. Like other β-blockers, atenolol relieves anginal pain by decreasing heart rate and cardiac contractility, which reduces myocardial oxygen demand. Although β-blockers also inhibit adrenergic-mediated coronary vasodilation, the resulting increase in coronary vascular resistance is overcome by the reduction in heart rate, which improves coronary perfusion by prolonging diastole. In addition to pharmacotherapy (which includes antiplatelet therapy, lipid-lowering therapy, and management of hypertension and diabetes), risk-reducing strategies (secondary prevention of CAD) include weight loss, smoking cessation, and aerobic exercise.

Calcium channel blockers, long-acting nitrates (e.g., isosorbide mononitrate), and ranolazine are alternative antianginal agents if there are contraindications to β-blockers or β-blockers do not provide adequate symptom control.

Calcium channel blockers (CCBs) such as diltiazem are the first-line treatment for vasospastic angina. CCBs are effective for both acute attacks and prophylaxis. In addition to CCBs, lifestyle modifications should be attempted, such as smoking cessation and abstaining from stimulants. Nitroglycerin is often used in the acute abortive treatment of vasospastic angina. Long-acting nitrates (e.g., isosorbide mononitrate) are only used as second-line agents for control of vasospastic episodes because the development of nitrate tolerance limits their long-term use.

Raynaud phenomenon is caused by an exaggerated vasoconstrictive response of the digital arteries and arterioles to cold or emotional stress. Raynaud phenomenon typically manifests with a sequential discoloration of fingers and/or toes, from white (ischemia) to blue (hypoxia) to red (reactive hyperemia). This patient most likely has vasospastic angina, which is associated with other vasospastic disorders, such as Raynaud phenomenon. The vascular theory of migraine postulates that dilation and vasoconstriction of intra- and/or extracranial vessels contribute to the development of migraine symptoms, such as headache and aura. While this theory is no longer widely supported, vasospasm may still play a role in the development of migraines and there may be an association of vasospastic angina with migraine.

Coronary artery vasospasm is the underlying mechanism of Prinzmetal angina. Episodes of Prinzmetal angina typically occur at rest (in contrast to exertional angina) and common triggers include stress, smoking, alcohol, illicit drugs (e.g., cocaine), and triptan use. The transient appearance of anterior ST-segment elevations and spontaneous resolution of symptoms in the setting of recent alcohol use and stress support this diagnosis.

Coronary CT angiography or cardiac stress testing is indicated for a patient with stable chest pain and an intermediate to high PTP of CAD. In patients with limited exercise capacity such as those who are frail or have an orthopedic disability, severe obesity (BMI > 40 kg/m2), COPD, or peripheral artery disease, pharmacological stress testing is the preferred option for stress testing. A substance that simulates the effect of exercise on the myocardium, i.e., dobutamine or a vasodilator (e.g., dipyridamole) is used in combination with cardiac imaging and ECG monitoring to detect evidence of stress-induced ischemic changes.

In patients with a low PTP of CAD, a shared decision-making approach that takes patient preferences, cost, and available resources at the setting of the care into consideration is recommended. Deferring testing for CAD (because patients at low risk may have false-positive results) and initiating a workup for other causes of chest pain is an appropriate step. Exercise ECG testing or coronary artery calcium scoring (using a non-contrast cardiac CT) may be reasonable alternative options in select patients. Cardiac stress testing with imaging or pharmacological stress is not required for patients with a low PTP of CAD.

Beta blockers (e.g., metoprolol) and calcium channel blockers (CCBs), especially the nondihydropyridine CCBs (e.g., verapamil), can affect the diagnostic value of cardiac exercise stress testing because they attenuate the chronotropic and inotropic effects of exercise. These medications may be withheld prior to testing at the clinician's discretion.

Methylxanthines (e.g., caffeine, theophylline) are competitive inhibitors of adenosine receptors and increase the risk of arrhythmias, which can hinder cardiac stress test completion or result interpretation. Discontinuation of methylxanthines should be considered also because the exercise stress test may need to be converted to a pharmacological stress test if the patient is unable to achieve a target heart rate with exercise. Methylxanthines decrease coronary vasodilation and thereby interfere with a pharmacological stress test using vasodilator agents (e.g., adenosine, dipyridamole).

Patients with stable chest pain and an intermediate to high PTP of CAD should undergo coronary CT angiography (CCTA) or cardiac stress testing (CST) for further risk stratification and treatment decisions. The goal of CST is to evaluate for stress-induced ischemic changes on ECG or cardiac imaging (stress echocardiography, myocardial perfusion imaging, or cardiac MRI). The stress is created by increasing heart rate and contractility (using exercise or dobutamine) or by inducing a coronary steal phenomenon (using vasodilators such as adenosine or dipyridamole). Reactive airway disease (e.g., asthma) is a contraindication for stress testing using adenosine or dipyridamole.

Coronary steal syndrome is myocardial ischemia caused by the redistribution of blood flow. The rigidity of severely stenotic arteries allows only a low coronary flow reserve. When coronary arteries dilate, blood is therefore diverted to healthier vessels and collaterals. Adenosine simulates stress by causing coronary vasodilation via the activation of adenosine A2A receptors. This leads to tissue ischemia distal to the stenosed coronary artery, manifesting as new ECG changes. As soon as the patient experiences chest pain and/or ST elevations are seen, the stress test should be terminated. Dipyridamole is another vasodilator that can be used during pharmacological stress tests to simulate the effect of exercise on the myocardium.

A cardiac stress test is typically performed to evaluate blood pressure, heart rate, and electrical conduction of the heart (using ECG) while the patient exercises under controlled conditions (usually on a treadmill) or after administration of a pharmacological agent to simulate cardiac stress (e.g., adenosine). Given his past medical history (stage 2 peripheral arterial disease) and 45 pack-years of smoking, this patient most likely has coronary heart disease. Coronary heart disease can manifest with gastrointestinal discomfort in the absence of retrosternal pain, especially in older individuals with diabetes mellitus. As in this patient, a resting ECG may not show evidence of cardiac ischemia. However, this patient is likely to have an abnormal result on cardiac stress testing (e.g., ST depressions), secondary to inadequate coronary artery perfusion.

In addition to cardiac work-up, this patient should also undergo endoscopic evaluation via esophagogastroduodenoscopy as abdominal discomfort and nausea can also be caused by gastroesophageal reflux disease and he has multiple risk factors for Barrett esophagus (male sex, age, obesity, smoking).

Congenital heart defects - Acyanotic

A VSD is an acyanotic congenital heart defect that initially has a left-to-right shunt. However, as blood flows through the defect into the right ventricle, blood flow through the pulmonary vasculature increases as well and over time results in increased pulmonary resistance and, ultimately, Eisenmenger reaction (shunt reversal). In this event, the defect becomes cyanotic and the peripheral oxygen saturation decreases. The body responds to chronic hypoxemia by increased erythropoietin production and a subsequent increase in red blood cells, i.e. polycythemia.

Failure of the ductus arteriosus to completely close postnatally allows blood to flow from the descending aorta back to the pulmonary artery (left-to-right shunt). In a large patent ductus arteriosus (PDA), this leads to volume overload of the right ventricle and the lung circuit. This increased blood flow causes pulmonary hypertension and irreversible remodeling of small pulmonary vessels, which may eventually lead to an Eisenmenger reaction (shunt reversal). This patient's palpable right parasternal heave and pronounced S2 are evidence of increased right heart strain. In patients with a large PDA, the features of differential cyanosis occur once shunt reversal develops. Because the ductus is located on the descending aorta distal to the origin of the left subclavian artery, reversal of the shunt results in deoxygenated blood reaching only the lower body. Due to the rise in pulmonary pressure, the characteristic continuous machine-like murmur heard in patients with PDA eventually disappears. Infants with PDA usually receive an infusion of indomethacin to induce closure of the duct, while in older children symptomatic PDAs are typically closed surgically or via percutaneous catheter occlusion. The presence of an Eisenmenger reaction is, however, a contraindication to a PDA closure.

Transthoracic echocardiography with agitated saline is the most appropriate next diagnostic step to evaluate for patent foramen ovale (PFO) showing a right-to-left shunt that increases with the Valsalva maneuver and coughing. PFO occurs in ~ 25% of individuals and is typically asymptomatic until complications due to right-to-left shunting arise. Transient increases in right atrial pressures allow emboli originating from the venous system (e.g., DVT) to pass directly from the right atrium into the left atrium, and then into the systemic and cerebral arterial circulation. Management of PFO after an embolic stroke includes surgical or percutaneous closure of the defect, antiplatelet agents or anticoagulation, and evaluation for other potential causes of stroke (e.g., arrhythmia, hypercoagulability, endocarditis). Paradoxical embolism can also be caused by a small atrial septal defect (ASD), which can be asymptomatic but typically manifests with a wide, fixed splitting of the second heart sound on auscultation. Echocardiography is also the first-line modality in the diagnosis of ASD.

CoA is most commonly located at the aortic isthmus, resulting in increased blood flow to the upper body and decreased blood flow to the lower body. Patients with noncritical CoA (i.e., mild-to-moderate CoA) typically present later in life (e.g., during childhood) with features of upper body hyperperfusion (e.g., high blood pressure in the upper extremities) and features of lower body hypoperfusion (e.g., cold feet, claudication upon exertion, brachial-femoral delay). In noncritical CoA, the left ventricular outflow obstruction leads to myocardial hypertrophy and increased collateral blood flow (e.g., to the intercostal arteries); rib notching occurs as a consequence of the collateral circulation between the internal thoracic and intercostal arteries and is usually a late finding (typically after 5 years of age). Doppler echocardiography is the confirmatory test of choice and should be performed in all patients with suspected CoA. It can identify the location and extent of the stenosis and show concurrent anomalies, such as a bicuspid aortic valve (present in ~ 60% of patients).

Pulmonary vascular resistance (PVR) is high in utero and decreases over the first few weeks of life. The progressive decrease in PVR and subsequent decrease in right ventricular pressure lead to increased left-to-right blood flow across the VSD. The enhanced shunting increases the overall volume of blood in pulmonary circulation, which causes increased lung perfusion (as evidenced by increased pulmonary vascular markings), increased pulmonary venous return to the left atrium, and left ventricular volume overload (resulting in left ventricular hypertrophy as evidenced on this patient's ECG and chest x-ray). These changes can lead to heart failure without cyanosis within the first few weeks to months of life, as seen in this child. If the VSD is not repaired and pulmonary blood flow continues to be high, vascular remodeling in later stages will cause PVR to increase again, resulting first in right ventricular hypertrophy and persistent pulmonary hypertension and, eventually, shunt reversal (Eisenmenger syndrome) resulting in heart failure with cyanosis.

Doppler echocardiography is the test of choice for diagnosing aortic coarctation. In addition to echocardiography, which provides dynamic imaging of the heart and can detect concurrent anomalies, Doppler helps to localize the coarctation and estimate its severity. This patient's clinical features such as features of arterial insufficiency in the lower extremities (e.g., intermittent claudication during physical activity, decreased femoral pulses), features of brachiocephalic hypertension (e.g., headache, epistaxis), and evidence of collateral circulation (rib notching on x-ray) are consistent with the presentation of aortic coarctation in adulthood. Moreover, this patient is now experiencing sequelae of untreated aortic coarctation such as left ventricular hypertrophy (as evidenced by her ECG findings) due to left ventricular outflow tract obstruction and dyspnea due to heart failure.

An increased risk of intracranial hemorrhage is present in patients with untreated aortic coarctation because of brachiocephalic hypertension. Moreover, aortic coarctation is associated with intracranial aneurysm formation (due to hypertension and/or genetic risk factors), which increases the risk of hemorrhage due to aneurysm rupture. Other complications of aortic coarctation include aortic arch aneurysm and dissection, coronary artery disease, ischemic stroke, endocarditis, left ventricular hypertrophy, and heart failure.

This patient's differential cyanosis and blood pressure differential between the upper and lower extremities, in conjunction with a systolic murmur over the left interscapular space (due to blood flow through the aortic narrowing), suggest coarctation of the aorta (CoA). In CoA, the narrowing of the thoracic segment of the descending aorta near the ligamentum arteriosum (aortic isthmus) causes an increased blood flow proximal to the narrowing and a decreased blood flow distal to the narrowing, resulting in blood pressure and oxygen saturation differentials like those seen in this patient. Newborns can remain asymptomatic until the closure of the ductus arteriosus (DA), after which there is an increase in left ventricular pressure and volume overload that results in heart failure.

Congenital heart defects - Cyanotic

Right axis deviation on ECG is typically seen in patients with TOF due to right ventricular hypertrophy. The thickened myocardium in the right ventricle produces increased electrical activity, which shifts the axis of cardiac depolarization. TOF also involves an overriding aorta, ventricular septal defect, and pulmonary stenosis. It is the most common congenital cyanotic heart lesion. In addition to these ECG findings, a chest x-ray showing a boot-shaped heart also supports the diagnosis. Echocardiography confirms the diagnosis.

TGA is a cyanotic heart condition that is associated with maternal diabetes (see “Commonly associated conditions and risk factors of cyanotic congenital heart defects” table). Mothers with untreated diabetes will have an elevated HbA1c. Other potential neonatal complications from maternal diabetes include macrosomia (seen in this patient), polycythemia, hypoglycemia, hypocalcemia, and respiratory distress syndrome. Alprostadil (PGE1) can be administered to this patient to help maintain a patent ductus arteriosus, which allows some oxygenated blood from the pulmonary veins to enter the systemic circulation through the aorta. This is a temporizing measure; surgical correction is the definitive treatment.

In patients with TOF, the right ventricular (RV) outflow obstruction due to central pulmonary valve stenosis and hypoplasia determines the severity of cyanosis and the intensity of the systolic heart murmur. Blood preferentially flows via the path of least resistance. When there is a high degree of RV outflow obstruction, blood will flow through the VSD instead of through the pulmonary artery for oxygenation in the lungs. As a result, deoxygenated blood will enter the left ventricle via the VSD and be pumped into the aorta and systemic circulation. If there is minimal RV outflow obstruction, blood will flow through the pulmonary vasculature, and become oxygenated before reaching the left ventricle, resulting in a reduction of cyanosis. In TOF, the single S2 can result from an attenuated pulmonary component (P2) that is often not heard on auscultation. Older children with TOF tend to squat during spells of hypoxia, which relieves symptoms by increasing systemic vascular resistance and, in turn, left ventricular outflow resistance. This creates higher left ventricular pressures, so that blood in the right ventricle will be directed through the pulmonary vasculature rather than the VSD. The increased blood flow across the RV outflow obstruction during squatting is also associated with an increased intensity of the ejection murmur.

Infants with tetralogy of Fallot frequently experience tet spells, which are thought to result from spastic contractions of the hypertrophic infundibular musculature at the transition from the right ventricle to the pulmonary artery. These contractions lead to severe right outflow tract obstruction, causing increased right-to-left shunting of deoxygenated blood through the VSD. Affected infants experience severe hypoxemia and profound cyanosis during tet spells and require immediate intervention. First-line treatment includes knee-chest positioning (older children can assume a squatting position) and administration of supplemental oxygen, which acts as a pulmonary vasodilator. Knee-chest positioning increases arterial oxygenation by increasing both systemic vascular resistance and left-sided heart pressures. This, in turn, decreases right-to-left shunting across the VSD and promotes blood flow into the pulmonary circulation rather than the aorta. Tet spells that are unresponsive to oxygen administration and knee-chest positioning are managed with IV morphine for sedation and fluids for volume expansion. If those measures fail to relieve the tet spell, IV beta blockers are administered to reduce sympathetic nervous system activity and infundibular musculature spasms.

In TVA, blood is unable to pass from the right atrium (RA) to the right ventricle (RV). Consequently, the RV is almost always hypoplastic. Venous blood, therefore, passes from the RA via an atrial septal defect (which, under these circumstances, is essential for survival) to the left atrium, where it mixes with oxygenated blood from the lungs. The mixed blood is pumped from the left ventricle (LV) into the systemic circulation (resulting in cyanosis) and pulmonary circulation (via a patent ductus arteriosus). LV hypertrophy occurs because the LV is single-handedly pumping blood through both the pulmonary and systemic circulation. A combination of RV hypoplasia and LV hypertrophy results in a severe left-axis deviation. Other findings that may be present on ECG include tall P waves (due to right atrial enlargement) and small R waves in the right precordial leads (e.g., V1, V2). The majority of patients with TVA also have a ventricular septal defect (VSD) and concomitant pulmonary outflow obstruction. The systolic murmur at the left lower sternal border arises from a VSD. In a patient with TVA, a single S2 that does not split with respiration indicates severely limited blood flow across the pulmonary valve and/or severe pulmonary stenosis. The systolic murmur of a VSD is softer with increasing severity of pulmonary stenosis and/or increasing size of the defect, because both result in a decreased pressure gradient across the VSD. Prostaglandin-E1 is given to maintain PDA patency (thereby increasing pulmonary circulation and blood oxygenation), but definitive treatment is staged surgical repair.

Congenital immunodeficiency disorders

The clinical presentation of DiGeorge syndrome is variable. Facial abnormalities are common and include micrognathia, cleft palate, a broad nasal bridge, a short philtrum, and low-set ears. Additionally, DiGeorge syndrome is associated with a variety of cardiac defects, including the otherwise rare truncus arteriosus defect (single overriding vessel seen on echocardiography). DiGeorge syndrome also involves impaired development of the parathyroid glands, leading to hypoparathyroidism and hypocalcemia, which may lead to tetany and seizures during infancy.

Cardiac myxoma

Cardiac myxomas are most commonly located in the left atrium. They may be pedunculated, in which case they often present with position-dependent symptoms of obstructed blood flow through the atrioventricular valves, or they may embolize systemically. Additionally, patients may present with constitutional findings (e.g., weight loss, fever, or anemia). The typical auscultatory finding (also present in this patient) is an early diastolic “plop”, caused by a movement of the mobile tumor mass, followed by a mid-diastolic rumbling murmur best heard at the apex that results from the obstructed blood flow through the mitral valve, and mimics the murmur of mitral stenosis. Echocardiography is the diagnostic test of choice to visualize the tumor and to assess its location, size, attachment, and mobility. The only definitive treatment of cardiac myxoma is surgical resection.

Chronic venous disease

Postthrombotic syndrome is a complication after deep vein thrombosis (DVT) that manifests unilaterally in the affected extremity and is characterized by chronic venous insufficiency. Features of postthrombotic syndrome include pain, swelling, pruritus, varicose veins, edema, and trophic skin changes. Symptoms are typically relieved by elevation of the legs. Venous ulcers are a complication of advanced posthrombotic syndrome and manifest as shallow lesions with irregular borders that typically cause pruritus and mild pain. Patients with mild disease are treated with lifestyle modifications (e.g., leg elevation) and compression therapy (e.g., compression stockings). Interventional procedures (e.g., endovenous thermal ablation) are used when conservative management with compression therapy fails or when complications (e.g., ulceration, trophic skin changes) are present.

Current guidelines recommend that all patients suspected to have CVD should undergo duplex ultrasonography before any treatment. The goal is to identify whether the patient has a correctable cause of venous reflux (e.g., reflux in the superficial venous system), and to plan for an interventional procedure (e.g., by identifying the superficial, deep, and perforator vein sites) if the patient qualifies for such a procedure. An initial trial of compression therapy is appropriate for patients with mild CVD (i.e., varicose veins or edema only) without a correctable cause, and pregnant patients with CVD. A patient with advanced CVD, as seen here, or a correctable cause of venous reflux should undergo endovenous thermal ablation as long as there are no contraindications to the procedure (e.g., deep vein thrombosis, peripheral artery disease). All patients with CVD should be counseled on lifestyle changes to improve venous return (e.g., daily exercise, frequent elevation of the legs, avoidance of long periods of standing and sitting).

Chronic venous insufficiency often leads to venous ulcers or mixed ulcers, classically appearing just above the medial ankle and associated with skin changes and unilateral edema. The location of this patient's ulcer, as well as the accompanying varicosity, skin color changes, and lower extremity edema make venous insufficiency the most likely primary etiology of this ulcer. This ulcer is likely a mixed ulcer because of this patient's cardiovascular history, diabetes, and smoking. Duplex ultrasonography (compression ultrasonography) is the first-line investigation in patients with features suggestive of CVI, as seen here. Evidence of venous reflux on duplex ultrasonography confirms the diagnosis of CVI. Duplex ultrasonography can help determine the course of treatment by identifying which valves are incompetent and assessing the patency of the previously thrombosed deep veins.

Bidirectional blood flow in the great saphenous vein on duplex ultrasonography, rather than the normal unilateral blood flow from the superficial to the deep system, is diagnostic of chronic venous insufficiency. Risk factors for chronic venous disease in this patient include female sex, family history of vascular disease (her father died from an ischemic stroke at a young age), pregnancy, obesity, and prolonged standing (i.e., work as a high school librarian). Elevated venous pressure leads to the incompetence of venous valves, causing reflux of blood into superficial veins, resulting in further elevation of venous pressure and the formation of varicose veins. Edema that worsens with standing and improves with leg elevation indicates progression of her venous disease due to damage to the capillary basement membrane. If this patient's chronic venous insufficiency remains untreated, she may develop chronic venous stasis ulcers. Conservative measures for chronic venous disease include compression therapy with compression stockings, frequent elevation of the legs, physical therapy, manual lymphatic drainage, and avoidance of heat and long periods of standing or sitting with bent legs.

Cardiovascular drug poisoning

In a patient with impaired renal function who is taking cardiac glycosides (e.g., digoxin), the development of diarrhea, vomiting, abdominal pain, palpitations, blurry vision, headache, and hyperkalemia suggests digitalis toxicity. Digoxin has a narrow therapeutic index and close monitoring of serum concentrations is necessary, especially in patients with kidney disease. Cardiac arrhythmias (premature ventricular contractions being the most common) are the most serious complication. If digitalis toxicity is suspected, the patient should be placed immediately on cardiac monitoring and an ECG should be obtained. Blood samples should also be drawn to evaluate electrolyte abnormalities and serum digoxin concentration. Patients with life-threatening arrhythmias (e.g., ventricular fibrillation), hyperkalemia, or end-organ dysfunction (e.g., altered mental status) should be treated immediately with digoxin-specific antibody fragments.

Intravenous glucagon is part of the initial treatment for symptomatic patients with beta blocker overdose with no response to IV fluids and atropine alone. Excessive beta-adrenergic blockade most commonly manifests as bradycardia and hypotension. In severe cases, profound myocardial depression and cardiogenic shock can occur. Glucagon increases intracellular cAMP by activating adenylate cyclase, which improves cardiac contractility while bypassing the beta receptors. Additional treatment depends on the severity of symptoms and may include administration of vasopressors (to correct hypotension), intravenous calcium (to treat cardiogenic shock), high-dose insulin (positive inotropic effect), and glucose (to treat hypoglycemia), and intravenous lipid emulsion therapy (to prevent further absorption of beta blocker).

Digoxin is a cardiac glycoside with inotropic and antiarrhythmic properties used in patients with heart failure and specific supraventricular tachyarrhythmias (e.g., atrial fibrillation). It primarily acts by blocking the Na+/K+ ATPase channel, resulting in decreased Na+/Ca2+ antiporter activity and increased inotropy. Digoxin also increases vagus nerve activity, which has a negative chronotropic effect and leads to PR prolongation with possible atrioventricular block. Pharmacodynamically, hypokalemia increases the risk of digoxin toxicity by enhancing its affinity for Na+/K+ ATPase. For this reason, predisposing factors for hypokalemia, such as loop diuretics and thiazide diuretics, should generally be avoided. Although it can increase serum potassium, spironolactone also predisposes the patient to digoxin toxicity because it decreases renal clearance of digoxin.

Cholesterol embolization syndrome

Atheroembolism is the embolization of multiple cholesterol crystals and atherosclerotic debris, usually to small and medium-sized arteries, following endovascular interventions (e.g., coronary angiography with stent placement), after the initiation of anticoagulant therapy, or spontaneously. Atheroembolism most commonly occurs in older individuals with multiple risk factors for atherosclerosis (e.g., hypertension, coronary artery disease, steatohepatitis, smoking). The embolization of microscopic cholesterol crystals into small arterioles affects many organs, and affected individuals can present with skin changes (e.g., livedo reticularis, blue toe syndrome), gastrointestinal ischemia, pancreatitis, CNS symptoms (transient ischemic attack, stroke), or acute kidney injury.

Cholesterol embolization syndrome typically affects older individuals with underlying atherosclerosis, particularly after invasive vascular procedures (e.g., cardiac catheterization, arteriography). Cholesterol crystals dislodge from atherosclerotic plaques and enter the bloodstream, blocking small to medium-sized arteries in various organs. Patients typically present with nonspecific systemic inflammatory features (e.g., fever, elevated ESR, eosinophilia) and various types of end-organ damage, depending on the embolism location (e.g., acute renal failure, peripheral skin manifestations such as livedo reticularis). The diagnosis is mostly clinical and may be supported by laboratory and imaging studies. In patients with renal manifestations, urine studies may show proteinuria, hematuria, and/or eosinophiluria. A kidney biopsy showing spindle-shaped vacuoles (intravascular cholesterol deposits) is the only definitive test to confirm the diagnosis, but it is not routinely performed. Treatment primarily focuses on prevention of recurrence and includes management of ASCVD and removal of the embolic source, e.g., in patients with abdominal aortic aneurysm.

In cholesterol embolization syndrome, ruptured plaque material can seed anywhere in the peripheral arteries, including the renal arteries, which subsequently impairs kidney function, manifesting as acute or subacute kidney injury. There is no specific treatment for cholesterol embolization syndrome. The mainstay of management is the prevention of recurrence, e.g., by optimizing the management of atherosclerotic cardiovascular diseases. Removal of the embolic source can be considered in consultation with a specialist. Options include surgical treatment (e.g., vascular bypass surgery, endarterectomy) and interventional treatment (e.g., angioplasty, endovascular stent grafting). Even with optimal treatment, the prognosis of cholesterol embolization syndrome remains poor.

Cardiac catheterization

Contrast-enhanced CT scan of the abdomen and pelvis should be performed in all hemodynamically stable patients with suspected retroperitoneal bleeding to confirm the diagnosis. While generally rare, retroperitoneal hemorrhage is the most common cause of unexpected mortality after diagnostic or interventional cardiac catheterization. It often occurs when femoral access is obtained above the inguinal ligament, as compression of the puncture site is difficult in this area and sufficient hemostasis is not easily achieved. Patients usually become symptomatic after significant blood loss, which often leads to a late diagnosis of the condition. Retroperitoneal hemorrhage can also occur spontaneously or after only mild trauma in patients on oral anticoagulants (e.g., warfarin). In hemodynamically unstable patients, the diagnosis is usually established clinically or with the help of ultrasound. Supportive treatment (e.g., monitoring, fluid resuscitation, blood transfusion, and normalization of coagulation factors if abnormal) is sufficient in most cases of retroperitoneal bleeding. In patients unresponsive to supportive treatment, endovascular treatment (e.g., intraarterial embolization or stent grafts) or open surgical repair may be necessary.

Cardiac arrest and cardiopulmonary resuscitation

Unsynchronized cardioversion (defibrillation) should be performed immediately in a patient with VF. VF is a life-threatening emergency and this patient's loss of consciousness indicates that he is already hemodynamically compromised. Although defibrillation is the only way to convert VF to sinus rhythm, administration of epinephrine, amiodarone, or lidocaine may be helpful adjuncts if the initial electrical shocks are not successful. Immediate initiation of high-quality chest compressions, minimizing interruption of chest compressions, and early defibrillation are the most important factors in improving patient survival.

The first step in any patient with PEA is the initiation of chest compressions. High-quality, uninterrupted chest compressions should be started immediately in any unresponsive patient without a pulse and are critical in the resuscitation of a patient with any type of cardiac arrest (regardless of the underlying rhythm). After chest compressions have been initiated, further resuscitative measures can be considered. There are a number of possible underlying etiologies for this patient's PEA arrest, including hypoxia, thromboembolism (myocardial infarction or pulmonary embolism), or pneumothorax (a complication of mechanical ventilation).

The next best step for this patient in PEA arrest is administration of epinephrine (given as 1 mg IV, and repeated every 3–5 minutes while continuing CPR). PEA arrest is characterized by continued electrical activity within the cardiac conduction system (as seen in this patient with sinus rhythm on the cardiac monitor) but inadequate cardiac output to support tissue perfusion. For this reason, PEA arrest is considered a nonshockable rhythm. High-quality chest compressions and IV epinephrine are vital aspects of management.

Amiodarone is an antiarrhythmic agent used in the management of shockable rhythms, i.e., refractory VF and pulseless ventricular tachycardia (VT). According to advanced cardiac life support guidelines, defibrillation is the first step in the treatment of shockable rhythms. If arrhythmia persists after the second defibrillation attempt, intravenous epinephrine should be administered and repeated every 3–5 minutes during resuscitation. Amiodarone is indicated after the third unsuccessful defibrillation attempt. Lidocaine is an acceptable alternative to amiodarone.

Carotid artery stenosis

Carotid artery stenosis (CAS) can manifest with monocular amaurosis fugax due to retinal ischemia, caused by stenosis-induced hypoperfusion, thrombosis, or microemboli. This patient has several risk factors for atherosclerosis (hypertension, hyperlipidemia, diabetes mellitus, smoking), and fundoscopic examination revealed cholesterol crystal emboli, which most commonly originate from carotid artery atheromas. Workup for patients with amaurosis fugax generally includes carotid duplex ultrasound to screen for CAS. Carotid revascularization is indicated for patients with symptomatic (e.g., those with amaurosis fugax), severe CAS, and should be considered for patients with symptomatic, moderate CAS, and asymptomatic patients with severe CAS.

Chemotherapeutic agents

Treatment with anthracyclines causes dose-dependent cardiotoxicity (most commonly left ventricular dysfunction or new-onset heart failure due to dilated cardiomyopathy) and requires monitoring of heart function before, during, and after treatment. Early detection of cardiotoxicity (e.g., ECG abnormalities, cardiac arrhythmias, ventricular dysfunction) is important for guiding therapy, as early manifestations are usually reversible. Cardiotoxicity can also develop after the completion of chemotherapy (sometimes years after treatment). For some patients, dexrazoxane can help prevent anthracycline-induced cardiotoxicity. Other common adverse effects of anthracycline chemotherapy include myelosuppression and alopecia. Treatment with cytarabine causes myelosuppression with megaloblastic anemia.

Carcinoid syndrome

The small intestine (especially the terminal ileum) is the most common location of a neuroendocrine tumor. A gastrointestinal neuroendocrine tumor with hepatic metastasis (or beyond) causes systemic symptoms of carcinoid syndrome, as large quantities of vasoactive metabolites (serotonin, histamine, VIP) circulate throughout the body without being degraded in the liver. In the heart, serotonin can cause endocardial fibrosis, resulting in carcinoid heart disease. In patients with carcinoid heart disease, the right side of the heart is typically affected as the lungs enzymatically inactivate the metabolites; therefore, the left side of the heart is usually spared. Increased serotonin metabolism explains this patient's elevated 5-HIAA levels and has resulted in pellagra (niacin deficiency), which classically manifests with the triad of diarrhea, dementia, and dermatitis. In patients with a metastasized neuroendocrine tumor with a patent foramen ovale, high amounts of tumor products pass directly from the right atrium to the left atrium, bypassing the pulmonary circulation, and causing damage to the left side of the heart.

Calcium channel blockers

Amlodipine is a dihydropyridine calcium channel blocker (CCB) often used in the treatment of hypertension. The primary mechanism by which dihydropyridine CCBs lower blood pressure is by causing peripheral arterial vasodilation, predominantly in the precapillary vessels. As a result, dihydropyridine CCBs use is often associated with peripheral edema. Other common side effects include headaches, dizziness, facial flushing, and reflex tachycardia. Dihydropyridine CCBs such as amlodipine cause systemic vasodilation, which increases hydrostatic pressure within precapillary blood vessels and can lead to peripheral edema. RAAS inhibitors, such as ACE inhibitors and ARBs, cause preferential vasodilation of the postcapillary blood vessels. When used in combination with CCBs, this results in the reduction of the transcapillary pressure and significantly reduces the risk of developing CCB-related peripheral edema.

Deep vein thrombosis

This patient presents with fever, leg pain, warmth, edema, and erythema, as well as a positive Homans sign, 3 days after delivery, which suggests a diagnosis of postpartum deep venous thrombosis (DVT). Compression ultrasonography confirms the diagnosis. Pregnancy is a hypercoagulable state; the risk of venous thromboembolisms reaches its peak in the first 6 weeks postpartum, when hypercoagulability is accompanied by endothelial injury (e.g., due to surgical delivery) and possibly venous stasis (e.g., due to immobilization after delivery). Smoking also increases the risk of DVT, as does delivery via cesarean section, maternal age > 35 years, and preterm delivery. LMWH, administered subcutaneously, is the initial treatment of choice because of its immediate antithrombotic effect and safety during breastfeeding. If no significant bleeding has occurred, it can safely be started 12 hours after cesarean section. Compression ultrasonography is the test of choice for diagnosing deep vein thrombosis. Given the patient's high risk of DVT (Wells score ≥ 3) and acute leg swelling with fever, DVT must be ruled out. D-dimer can only be used to rule out DVT when pretest probability is low (Wells' DVT score = 0).

Duplex ultrasonography should be performed in patients with ST who have risk factors for deep venous thrombosis (DVT), such as pregnancy, chronic venous insufficiency, and obesity. While ST is typically a clinical diagnosis, duplex ultrasonography can be used to assess for concomitant DVT and evaluate the extent and location of ST, which help determine the need for anticoagulation. Most cases of ST are self-limited and management is symptomatic, usually consisting of NSAIDs (however, NSAIDs should be avoided during pregnancy), elevation of the affected limb, and compression therapy. Anticoagulation is recommended for patients with a large segment (≥ 5 cm) ST or a thrombus near the deep venous system, and/or if risk factors for DVT are present. Low molecular weight heparin is preferred in pregnant patients.

Catheter-related thrombosis should be suspected in any patient with an indwelling catheter who presents with findings of deep venous thrombosis (DVT) on the same side as the catheter. DVT is more common in patients with risk factors that enhance the pathophysiological mechanisms of the Virchow triad: hypercoagulability (e.g., active cancer, thrombophilias), endothelial injury (e.g., intravascular devices), and venous stasis (e.g., immobilization). The diagnostic approach to DVT should be based on pretest probability (PTP), which can be determined using the Wells criteria for DVT. Individuals with low PTP should be screened with D-dimer to rule out DVT while individuals with a high PTP or a positive D-dimer should receive a venous compression ultrasound. Primary treatment consists of oral anticoagulation therapy.

Tumors may produce proteins and cytokines with thrombophilic effects and malignancy must be considered a possible underlying cause in patients with DVT. In patients with an unprovoked DVT, DVT in unusual locations, or recurrent DVT, workup should include a limited cancer screening with a thorough history and physical examination, certain basic laboratory studies (a complete blood count, liver function tests, serum calcium, urinalysis) and screening for colon, prostate, breast, and cervical cancer as appropriate for age and sex. Extensive cancer screening (e.g., using abdomen or pelvic CT scans, upper GI endoscopy) is not routinely recommended. The US Preventive Services Task Force recommends colon cancer screening in all adults between 45 and 75 years. The recommended screening interval when using colonoscopy is 10 years; this patient is due for a colonoscopy because his last screening was 11 years ago (see "Screening for cancer" table).

An inferior vena cava filter is indicated in this patient to prevent pulmonary embolism. IVC filters are indicated in patients with (or at high risk of) thromboembolism who have absolute contraindications to anticoagulation (e.g., recent surgery, intracranial hemorrhage, active bleeding), or complications from anticoagulation, as well as those who have not responded to anticoagulation. This patient underwent a craniotomy and evacuation of a subdural hematoma four days ago. Because of the risk of secondary hemorrhage, anticoagulation is contraindicated.

Dilated cardiomyopathy

This patient presents with features of dilated cardiomyopathy, most likely caused by his chronic alcohol use. Alcohol has toxic effects on the myocardium, leading to ventricular dilation and reduced contractility. If detected early enough, consistent abstinence from alcohol leads to reversal of cardiomyopathy and is, therefore, the most important step in management. In patients with chronic alcohol use disorder, the shift to abstinence should be monitored closely to prevent complications of alcohol withdrawal. Dilated cardiomyopathy and supraventricular tachyarrhythmias often occur concomitantly. Supraventricular tachyarrhythmia can both lead to and result from dilated cardiomyopathy, and determining which condition came first can be difficult. However, considering the absence of any cardiac murmurs and preexisting cardiac conditions in this patient, a diagnosis of tachycardia-induced cardiomyopathy is most likely. Tachycardia-induced dilated cardiomyopathy usually resolves with treatment of the underlying arrhythmia (typically within 3 months).

Down syndrome

Atrioventricular septal defects (AVSD; also referred to as endocardial cushion defects) are the most common congenital heart defects in patients with Down syndrome, occurring in about 40% of newborns with trisomy 21. AVSDs are usually diagnosed in the prenatal period, and discovery of an AVSD should warrant prompt genetic testing, as there is a strong association with trisomy 21. Down syndrome is diagnosed in approx. 40–50% of children with AVSD. Diuretics, inotropic agents, and ACE inhibitors are usually given to improve cardiac function. Definitive treatment consists of complete surgical repair.

Diabetes medications

Metformin is associated with an increased risk of life-threatening lactic acidosis in patients with predisposing conditions that reduce lactic acid clearance (i.e., renal and/or hepatic insufficiency), increased lactic acid production (e.g., sepsis), or a combination of both (e.g., heart failure with low cardiac output). This patient's renal insufficiency and HF with decreased cardiac output are both contraindications to metformin therapy, which should therefore be discontinued immediately. Insulin should instead be used for inpatient glycemic control. The use of metformin may be safe in the case of chronic HF with preserved cardiac output. Other important indications for discontinuing metformin (albeit temporarily) are surgery, acidemia, and the intravenous administration of an iodinated contrast medium (e.g., CT scans, fluoroscopic studies).

Diuretics

Thiazide diuretics such as hydrochlorothiazide act by inhibition of the sodium-chloride symporter in the distal convoluted tubule, which results in blood pressure reduction. In the treatment of hypertension, thiazide diuretics are used as first-line agents. When additional antihypertensives such as ACE inhibitors are initiated, patients who already take other antihypertensive medications such as diuretics or are volume-depleted are at higher risk for first-dose hypotension. While this patient has normal electrolytes, possible side effects of thiazide diuretic include hypokalemia, hyponatremia, and hypomagnesemia.

Esophageal atresia

A vascular ring is a rare cause of respiratory symptoms in infants that is treated with surgical division. Vascular rings typically manifest with shortness of breath, wheezing, stridor due to tracheal compression, as well as difficulty swallowing, regurgitation of food, and/or unintended weight loss resulting from esophageal compression. The severity of symptoms depends on the degree of tracheal and esophageal compression by the vascular ring. X-ray typically shows tracheal bowing and narrowing, indicating tracheal compression.

Fibromuscular dysplasia

CT angiography is a noninvasive imaging method that has high accuracy in confirming the diagnosis of fibromuscular dysplasia. Imaging would typically show a single or multiple stenoses of the renal arteries. Other imaging methods that can be used to diagnose FMD are duplex ultrasonography and magnetic resonance angiography. The choice of method depends mostly on expertise and availability at individual institutions. After this patient's blood pressure has been adequately controlled and the diagnosis has been confirmed, the renal artery stenosis should be treated with percutaneous transluminal angioplasty.

Hypertension

Hypertensive nephrosclerosis results from renal vascular injury secondary to long-standing arterial hypertension. Sclerosis in the capillary tufts and hyaline arteriolosclerosis, as seen on kidney biopsy, are caused by chronic damage from increased capillary hydrostatic pressure in the glomeruli as well as ischemic damage from progressive narrowing of the renal arterioles. Patients with nephrosclerosis present with elevated blood pressure and laboratory findings that suggest impaired renal function, including elevated BUN and creatinine and presence of proteinuria. Some patients may also have microangiopathic hemolytic anemia. Ultrasound typically shows small, atrophic kidneys. Patients with hypertensive nephrosclerosis initially have microalbuminuria but eventually develop macroalbuminuria as the disease progresses.

Isolated systolic hypertension is caused by decreased arterial elasticity and compliance associated with aging. This condition most commonly occurs in adults aged over 60 years and typically manifests with wide pulse pressure. Patients with isolated systolic hypertension have a high risk of renal dysfunction and cardiovascular events, e.g., myocardial infarction, stroke. In a patient with both hypertension and a history of migraine requiring prophylactic therapy, beta blockers (e.g., propranolol) are an adequate first-line alternative as they target both conditions. In patients with hypertension and no other comorbidities, thiazide diuretics, ACE inhibitor, calcium channel blockers, and/or angiotensin-receptor blockers should be tried first, before administering a beta blocker.

Hypertensive crises

Immediate intervention is required to reduce the blood pressure and prevent (further) end-organ damage in this patient with a hypertensive emergency. Preferred agents include IV nitroprusside, labetalol, or nicardipine. Nitroprusside, in particular, is widely used because of its quick onset (< 1 min) and broad applicability to various hypertensive emergency syndromes. It is important to reduce blood pressure slowly, i.e., by a maximum of 25% within the first hour, to prevent coronary insufficiency and to ensure adequate cerebral perfusion. Nitroprusside reduces renal perfusion and should be avoided in patients with acute renal failure.

Patients with hypertensive crises should be immediately evaluated for acute signs and symptoms of end-organ damage to differentiate hypertensive urgency from hypertensive emergency and to determine if rapid reduction in blood pressure is required. This patient's confusion (i.e., altered mental status manifesting with disorientation) is most likely due to hypertensive encephalopathy or stroke, indicating acute end-organ damage in the central nervous system. Patients with hypertensive emergencies should be immediately admitted for intravenous antihypertensive therapy and critical care. Other clinical features of hypertensive emergency include cardiac symptoms (e.g., dyspnea, chest pain), acute kidney injury, acute hypertensive retinopathy, and microangiopathic hemolytic anemia.

Hypertrophic cardiomyopathy

Metoprolol and other beta blockers are first-line agents for patients with hypertrophic cardiomyopathy (HCM). Beta blockers provide rate control, which allows for a longer diastole and greater diastolic filling. In addition, these drugs reduce contractile force, which leads to a reduced left ventricular outflow tract pressure gradient and reduced myocardial oxygen demand. Furthermore, refraining from intense physical exercise is indicated in all patients with this condition, even those receiving pharmacotherapy, because of the increased risk of sudden cardiac death. Primary prophylactic ICD placement should be considered in patients with a family history of HCM-related sudden cardiac death and/or syncope. Diagnosis of hypertrophic cardiomyopathy (HCM), the most likely cause of this patient's presentation, can be confirmed by echocardiography which typically shows systolic anterior motion of the anterior mitral valve leaflet, asymmetrical septal hypertrophy, and septal wall thickness of >15 mm. Doppler echocardiography can reveal increased left ventricular outflow tract pressure gradients.

Interventricular septal hypertrophy is seen in patients with hypertrophic obstructive cardiomyopathy and is the most common cause of sudden cardiac death in athletes under the age of 30. The condition is often asymptomatic but can cause life-threatening arrhythmias and sudden death. A systolic ejection murmur that increases with valsalva maneuver and standing and decreases with hand grip, squatting, or lying down can be an important clue toward the diagnosis.

Placement of an automated implantable cardioverter defibrillator (AICD) is the best method to prevent sudden cardiac death (SCD) in patients with HOCM and a history of sudden cardiac arrest or sustained ventricular tachycardia. Other indications for AICD placement in patients with HOCM include a positive family history of SCD in a close relative ≤ 50 years of age, syncope of unknown cause, left ventricular (LV) wall thickness ≥ 30 mm, LV apical aneurysms, and LV systolic dysfunction. Patients with HOCM who are not in any of these categories still require risk stratification for AICD placement because of the high risk of SCD associated with this condition. Beta blockers are the first-line therapy for the symptomatic treatment of patients with HOCM. Other therapy options include nondihydropyridine calcium channel blockers, septal myectomy, and cardiac pacemaker. High-dose diuretics, spironolactone, and digoxin should generally be avoided. It is important to note that these treatment options are not known to reduce the risk of premature death in patients with HOCM.

Hypertrophic cardiomyopathy (HCM) manifests with an area of increased left ventricular wall thickness that is typically asymmetrical and involves the septum or anterolateral LV wall. Along with mitral valve and papillary muscle abnormalities, septal hypertrophy can lead to left ventricular outflow tract obstruction, resulting in exertional syncope and a systolic ejection murmur. Although the systolic murmur in patients with HCM does not significantly radiate into the carotid arteries, left ventricular outflow tract obstruction in obstructive HCM may mimic an aortic stenosis murmur and may be heard as a subtle ejection murmur on auscultation of the carotids. The ECG shows high voltage QRS complexes, indicating left ventricular hypertrophy. HCM is most commonly a hereditary condition, which explains the history of sudden cardiac death in this patient's father. The intensity of the murmur associated with HCM decreases with maneuvers that increase venous return (e.g., rapid squatting) because they increase preload, which in turn decreases the pressure gradient across the obstruction. This change in murmur intensity can help differentiate HCM from other causes of systolic murmurs, such as ventricular septal defect and mitral regurgitation.

Hypertrophic cardiomyopathy (HCM) is the most common hereditary heart disease and may be obstructive or non-obstructive. HCM may be asymptomatic or manifest with exertional dyspnea, syncope (as in this patient), cardiac arrhythmias, heart murmurs, or sudden cardiac death (particularly during or after intense physical activity). As is the case here, HCM is typically associated with a harsh crescendo-decrescendo systolic ejection murmur at the left lower sternal border that increases in intensity with maneuvers that decrease left ventricular filling (Valsalva maneuver and standing) and decreases in intensity with maneuvers that increase left ventricular filling (squatting or passive leg elevation). Patients with HCM may also have an accompanying murmur of mitral regurgitation (i.e., a holosystolic murmur best heard at the apex), which is caused by systolic anterior motion of the mitral valve (SAM) leaflets into the left ventricular outflow tract. Echocardiography is the best initial and confirmatory test.

Heart failure

Chronic uncontrolled hypertension is the most common cause of HFpEF. Chronic hypertension increases the afterload against which the left ventricle (LV) contracts. As a compensatory mechanism, the myocardium undergoes concentric hypertrophy to maintain cardiac output. Over time, the compensatory response of LV thickening is associated with the maladaptive change of interstitial myocardial fibrosis, which leads to an increase in LV stiffness and impaired myocardial relaxation. As a result, patients develop an increase in left ventricular filling pressures and reduced ventricular filling with normal ventricular contraction (i.e., diastolic dysfunction). Severe myocardial fibrosis can ultimately impair myocardial contractility and result in systolic dysfunction but in such a scenario, the patient will have a low ejection fraction. Note that impaired myocardial relaxation could have also been correct for restrictive cardiomyopathy, in which the ventricular walls harden without myocardial hypertrophy.

Mineralocorticoid receptor antagonists (MRAs), such as eplerenone, are associated with improved prognosis (i.e., reduced morbidity, mortality, and hospitalization rates) in patients with HF. MRAs are indicated for patients with ACC/AHA stage C HFrEF without contraindications (i.e., eGFR < 30 mL/min/1.73 m2 and serum K+ > 5.0 mEq/L). Other drugs that improve prognosis in patients with HF include beta blockers, ACE inhibitors, angiotensin receptor-neprilysin inhibitors (ARNIs), hydralazine with isosorbide nitrate, and SGLT2 inhibitors. This patient should be switched from lisinopril (an ACE inhibitor) to an ARNI (ARNIs are associated with a greater reduction in mortality and hospitalization rates), and a beta blocker should be added to maximize medical therapy. Beta blockers should be used with caution in the acute management of HF as they can worsen the condition.

Arterial hypertension (HTN) is one of the most common causes of CHF. Chronic HTN causes long-term concentric hypertrophy of the left ventricle and, if left untreated, can ultimately result in left-sided heart failure, which manifests with symptoms of pulmonary congestion (e.g., exertional dyspnea, orthopnea, bibasilar crackles), tachycardia, and S4 heart sound. Long-term left-sided heart failure may eventually progress to right-sided heart failure as a result of chronic volume overload and manifest with symptoms of fluid retention (e.g., peripheral edema, jugular venous distention). Although this patient's blood pressure is only mildly elevated, it is most likely attributed to the backflow of blood into the right chambers of the heart and a consequent decrease in left ventricular output.

This patient's acute onset dyspnea and CXR findings suggest cardiogenic pulmonary edema due to left ventricular failure. Individuals with left ventricular failure initially develop interstitial edema, which results in smooth reticular opacification and Kerley B lines due to accentuation of the vascular markings. With the further increase in pulmonary capillary wedge pressure, individuals can develop features of alveolar edema (e.g., consolidation with an air bronchogram) and pleural effusion (e.g., blunting of the costophrenic angle). In pulmonary edema, the opacification can often assume a perihilar distribution (a so-called "batwing" or "butterfly-shaped" pattern), which is seen here, because the periphery of the lung has better lymphatic drainage than the central regions.

Elevated levels of brain natriuretic peptide (BNP) and the presence of an S3 gallop both indicate increased ventricular filling pressures, which is seen in heart failure (HF). BNP, which is released in response to stretching of the cardiac ventricle, is a sensitive parameter to evaluate patients with symptoms of HF. High levels of BNP (> 400 pg/mL) in patients with classic symptoms of HF have a high positive predictive value and are associated with a worse prognosis, while low values (< 100 pg/mL) in patients with dyspnea have a high negative predictive value for HF.

In systolic dysfunction, poor contractility leads to decreased stroke volume and cardiac output. In response to decreased cardiac output, there is compensatory activation of the RAAS and sympathetic nervous system, resulting in increased TPR. In addition, incomplete ventricular emptying during systole results in left ventricular volume overload, which results in increased LVEDV. Increased LVEDV and poor forward flow cause increased left ventricular pressure, which is transmitted to the left atrium, resulting in increased PCWP.

Arteriovenous (AV) fistulas cause a decrease in peripheral vascular resistance because they allow shunting of blood from high-pressure arterial circulation to the low-pressure venous system. This shunting causes a decrease in systemic vascular resistance, which results in elevated heart rate and decreased effective circulating volume, thereby triggering activation of the renin-angiotensin-aldosterone system (RAAS). RAAS activation, in turn, causes retention of sodium and water, resulting in increased cardiac filling pressures with elevated cardiac output, which may culminate in a state of high-output heart failure (high-output HF). This patient requires immediate surgical division of the fistula to reverse current symptoms and prevent irreversible myocardial damage. Other common causes of high-output HF include pregnancy, anemia, hyperthyroidism, and wet beriberi.

The reduced CO seen in CHF results in organ hypoperfusion, which also affects the kidneys. Reduced renal blood flow leads to compensatory activation of the RAAS system. Angiotensin II causes vasoconstriction of the afferent and efferent arterioles within the kidney, decreasing the net renal blood flow. Vasoconstriction is, however, more pronounced in the efferent arteriole, which results in an increase in intraglomerular pressure to maintain the glomerular filtration rate. In combination with the other effects of RAAS activation (aldosterone-induced renal Na+/H2O resorption and systemic vasoconstriction), this maintains CO. Although RAAS activation is a compensatory mechanism to maintain the CO in patients with CHF, prolonged renal hypoperfusion (particularly in conjunction with precipitating factors, such as NSAID use and dehydration) can lead to renal insufficiency.

In addition to supplemental oxygen therapy and ventilatory support as needed, this patient requires IV furosemide therapy to improve his volume overload status. Loop diuretics are a first-line treatment for symptomatic relief in acute exacerbation of congestive heart failure in patients with normal or elevated blood pressure. To assess the response to therapy and prevent excessive diuresis and preload reduction, it is important to monitor for adverse effects such as hypokalemia and hyponatremia as well as weight changes and volume status. Intravenous vasodilators (e.g., nitroglycerine, nitroprusside) can be considered as an adjunct treatment. These agents cause peripheral vasodilation, resulting in pooling of blood in the venous system, which rapidly reduces ventricular filling pressures and improves cardiac function.

Signs of systemic venous congestion (JVD and bilateral lower extremity edema) and reduced right heart output (dyspnea on exertion with clear lungs on auscultation) are consistent with right heart failure. This patient's right ventricular failure is likely due to recurrent malignancy-associated pulmonary embolism, which leads to an increase in pulmonary artery pressure and right ventricular afterload. Over time, this increased ventricular afterload induces right heart remodeling with consequent right ventricular dysfunction. In severe cases, patients may also develop features of hepatic congestion (e.g., abdominal distention, jaundice, and ascites) and/or gastric congestion (e.g., nausea and early satiety). Management of decompensated right heart failure includes oxygen therapy (if the patient is hypoxemic), fluid restriction, diuretic therapy, and treatment of any underlying cause.

Assessing HJR can help distinguish cardiac disease from hepatic disease in a patient presenting with bilateral lower extremity edema and ascites. A positive HJR indicates impaired relaxation of the right ventricle and consequent inability to accommodate an increased venous return to the heart. The most common causes of this finding include restrictive cardiomyopathy, constrictive pericarditis, and right ventricular heart failure (e.g., due to myocardial infarction). This patient further presents with features suggestive of hemochromatosis: symmetric arthropathy of the 2nd and 3rd metacarpophalangeal joints, fatigue, abdominal pain, and hepatomegaly. These findings indicate that he has restrictive

cardiomyopathy as a result of iron deposition in the heart, which ultimately causes congestive hepatopathy (cardiac cirrhosis).

Under normal conditions, ADH secretion is tightly controlled by serum osmolality. But in patients with CHF, nonosmotic stimuli for ADH secretion (e.g., increased baroreceptor firing) become more relevant, and ADH secretion increases due to the decrease in cardiac output (CO). Increased ADH leads to increased reabsorption of free water, which, in turn, results in hyponatremia due to fluid dilution in the extracellular fluid compartment. A decrease in serum sodium is therefore closely associated with a decrease in CO in patients with heart failure. Both diuretics and ACE inhibitors can cause hyponatremia but they are still recommended for patients with CHF because they increase free water elimination and improve cardiac function.

Heparin-induced thrombocytopenia

As evidenced by his increased aPTT and normal PT, this patient was given subcutaneous heparin for deep vein thrombosis prophylaxis. Heparin-induced thrombocytopenia (HIT), formerly called type 2 HIT, is a rare, immune-mediated adverse effect of heparin. The risk of developing this condition is higher with unfractionated heparin but can also occur in patients treated with low molecular weight heparin. HIT typically occurs 5–14 days after initiation of heparin and can result in thrombotic events (e.g., arterial occlusion). Although HIT is characterized by thrombocytopenia, bleeding manifestations are rare as the platelet count rarely decreases below 20,000 platelets/mm3. The diagnosis is confirmed by serum immunoassays to detect anti-heparin/platelet factor 4 antibodies but heparin should be immediately stopped without waiting for diagnostic confirmation and nonheparin anticoagulation should be initiated. HIT should be differentiated from the more common nonimmune heparin-associated thrombocytopenia (formerly called type 1 HIT), which occurs within 5 days of heparin initiation and is a transient, clinically insignificant, mild to moderate thrombocytopenia that can be managed with serial monitoring of platelet counts and does not require discontinuation of heparin.

Hemochromatosis

This patient has evidence of multiorgan involvement: dilated cardiomyopathy, arthritis (usually symmetrical, oligoarticular, progresses to chondrocalcinosis), hepatomegaly, hyperpigmented skin, and diabetes (bronze diabetes). These features indicate a diagnosis of hereditary hemochromatosis (primary iron overload), which is the most frequent genetic disease in the White population. Regular phlebotomy to deplete iron stores is the treatment of choice for patients with hereditary hemochromatosis. After confirming the diagnosis, therapeutic phlebotomy should be started immediately in patients with symptomatic disease or evidence of iron overload (serum ferritin > 1000 ng/mL), as this can reverse early left ventricular systolic dysfunction and minimize damage to other organs.

Hemochromatosis causes iron deposition in the cardiac conduction system, which can lead to a variety of conduction abnormalities. These include sinus node dysfunction, complete AV block, atrial and ventricular tachyarrythmias, and rarely, sudden cardiac death. The most common arrhythmia observed in patients with hemochromatosis is paroxysmal atrial fibrillation. Other common cardiac complications include dilated cardiomyopathy, restrictive cardiomyopathy, and heart failure.

Infective endocarditis

This patient with acute IE has most likely acquired S. epidermidis bacteremia through an infected peripheral venous catheter during her hospital stay. S. epidermidis has the ability to adhere to foreign bodies (e.g., intravenous catheters, pacemakers) and subsequently form a biofilm. The pathogen accounts for about 30% of health care-associated bloodstream infections and is a common cause of IE in patients with prosthetic heart valves. Because coagulase-negative staphylococci often colonize the skin of healthy individuals, they are commonly found in contaminated blood cultures, and their presence is not always clinically significant. Repeat cultures and evaluation of the culture results in accordance with clinical findings are therefore recommended.

The patient has acute aortic regurgitation and subsequent left-sided heart failure from IE, which together are an indication for surgical intervention. Further indications for surgical treatment of IE include uncontrolled infection, systemic embolization, prosthetic valve endocarditis, or fungal endocarditis. Mechanical valve replacement is the treatment of choice in a young (< 65 years of age) patient without contraindications for anticoagulation. Patients with current bleeding, history of intracranial hemorrhage, coagulopathy, or severe thrombocytopenia (< 50,000/µL) should be evaluated for porcine valve replacement as mechanical valves require lifelong anticoagulation.

Perivalvular thickening with an echolucent cavity indicates perivalvular abscess formation, a severe complication of IE that develops when infection spreads to the valve annulus and/or cardiac septum. Conduction abnormalities on ECG (e.g., AV block) occur when the abscess extends to cardiac conduction tissues, and they are most commonly seen in patients with aortic valve involvement. Perivalvular abscess is associated with high mortality if left untreated, as well as additional complications such as systemic embolization and acute coronary syndrome (due to coronary compression). Always suspect a perivalvular abscess in patients with IE who develop a new conduction abnormality.

This child fulfills 5 of the minor Duke criteria for the diagnosis of infective endocarditis (IE): a predisposing heart abnormality (ventricular septal defect), fever ≥ 38°C (100.4°F), vascular phenomena (splinter hemorrhages, Janeway lesions), immunologic phenomena (glomerulonephritis manifesting with nephritic syndrome, Roth spots), and a positive blood culture for a microorganism consistent with infective endocarditis (≥ 2 positive cultures are required to qualify as a major criterion). Viridans streptococci like S. sanguinis typically cause subacute endocarditis with an insidious onset over weeks to months and are common endocarditis pathogens in children with structural heart defects.

Staphylococci such as S. aureus account for the majority of cases of healthcare-associated IE. IE caused by S. aureus is characterized by acute onset of symptoms and rapid progression (hours to days). Acute IE due to S. aureus can quickly lead to complications such as valvular insufficiency, heart failure, and septic emboli. Therefore, in addition to removing the infected CVC, empiric antibiotic therapy (vancomycin plus beta-lactam for native valve endocarditis) should be initiated after obtaining blood cultures. Coagulase-negative staphylococci (e.g., S. epidermidis), S. aureus, enterococci, and Candida spp. are the organisms most commonly associated with CLABSI. Note that IE associated with coagulase-negative staphylococci typically has a subacute course with an insidious onset (weeks to months), low-grade fever, and nonspecific symptoms, unlike the fulminant course seen in this patient.

Septic pulmonary embolism is a common and severe complication of right-sided IE and is caused by bacterial thromboemboli that form on the affected heart valve and dislodge into the lung. Patients present with cough, pleuritic chest pain, and nodular pulmonary infiltrates. While tricuspid valve IE is rare, nonsterile injections (e.g., in individuals who use IV drugs) leading to bacteremia as well as indwelling intravascular devices increase the risk for this condition. Peripheral disease manifestations (e.g., Roth spots, Janeway lesions, embolic arterial occlusion of the kidney, brain, and spleen) are not typically seen in right-sided IE.

Streptococcus gallolyticus can be found in the normal bowel flora of healthy humans. A link between S. gallolyticus bacteremia, particularly in endocarditis, and colorectal cancer has been well established. However, it remains unclear whether this pathogen is part of the etiology of colorectal malignancies or a consequence of the disease. A colonoscopy is indicated in all patients with S. gallolyticus on blood culture. In a patient with suspected IE, a minimum of three blood cultures from different venipuncture sites should be obtained as soon as possible and over a short period of time (e.g., < 1 hour in acutely ill patients). The presence of bacteria typical for IE (e.g., Staphylococcus aureus) obtained from two separate blood cultures is a major Duke criterion. Because patients with IE usually have continuous bacteremia, blood cultures are positive in a high percentage of cases. Blood cultures should always be collected before initiating antibiotic therapy, so as to avoid potentially false-negative results.

Staphylococcus aureus is the most common cause of acute IE in almost all groups of patients, including individuals who inject drugs, and the most common cause of right-sided IE. Other notable causative pathogens of IE associated with IV drug use include Staphylococcus epidermidis and fungi (e.g., Candida spp.). Subacute IE, which is characterized by an insidious onset (weeks to months) and less severe constitutional symptoms (e.g., low-grade fever), is most commonly caused by viridans streptococci.

This patient presents with signs and symptoms of acute infective endocarditis (IE), including fever, Janeway lesions, petechiae, a new heart murmur, hematuria (> 3 RBC on urinalysis) indicating renal injury, and Roth spots. Neurological complications of IE, such as ischemic stroke, intracerebral hemorrhage, and/or cerebral microabscesses, are often caused by septic emboli to the brain. Up to 40% of patients with IE experience symptomatic neurological complications, and up to 80% have embolic findings on brain imaging. This patient's extensive neurological findings indicate involvement of multiple brain areas. Thrombolytic therapy is not recommended for patients with IE and embolic stroke because of the risk of cerebral hemorrhage. Empiric antibiotic treatment, which reduces the risk of recurrent embolism, should be initiated after collecting three sets of blood cultures. Moreover, evaluation of the brain with a noncontrast CT is indicated to rule out hemorrhage. Cardiothoracic surgery may be necessary for complicated IE.

Enterococci are a common cause of IE following nosocomial UTIs. E. faecalis is especially virulent and is more likely than E. faecium to progress to bacteremia and endocarditis. Because penicillin resistance varies within the group of enterococci, combination therapy (e.g., ampicillin plus gentamicin) is recommended in the treatment of enterococcal endocarditis.

Intravenous vancomycin therapy is the initial empiric antibiotic treatment in patients with native heart valves and suspected IE because its coverage includes MRSA. Empiric therapy is typically administered right after blood cultures are drawn.
The intravenous antibiotics should be adapted according to resistogram results from blood cultures. In intravenous drug users in which MRSA is not the causative pathogen, shorter 2-week antibiotic regimens with either intravenous nafcillin or oral cloxacillin can be considered.

Viridans streptococci, such as S. sanguinis, are the most common cause of subacute IE in damaged native heart valves (e.g., bicuspid aortic valve). Because viridans streptococci are part of the normal oral flora and can be introduced into the blood following dental procedures, patients with certain types of congenital heart disease (e.g., unrepaired cyanotic heart defects) should receive antibiotic prophylaxis prior to invasive dental procedures.

Coagulase-negative staphylococci (e.g, S. epidermidis), which have the ability to adhere to foreign bodies and form a biofilm, are a common cause of early-onset prosthetic valve IE (i.e., ≤ 12 months following surgery). IE due to S. epidermidis typically has an insidious onset with a subacute disease course, as seen here. Staphylococcus aureus, another leading cause of prosthetic valve IE, typically causes acute disease with high fever, and severe constitutional symptoms.

Intravenous therapy with nafcillin and rifampin for at least 6 weeks in combination with gentamicin for 2 weeks is the treatment of choice for prosthetic valve IE due to methicillin-susceptible staphylococci. Treatment with gentamicin is restricted to 2 weeks because the risk of renal toxicity increases with duration of therapy. Prosthetic valve IE generally requires a longer duration than native valve IE. Prosthetic valve IE caused by methicillin-resistant staphylococci should be treated with an intravenous combination of vancomycin, rifampin, and gentamicin.

Third-generation cephalosporins, such as ceftriaxone, have a broad spectrum coverage against gram-negative bacteria and are the treatment of choice for infective endocarditis caused by HACEK organisms. Alternative treatment regimens include fourth-generation cephalosporins, fluoroquinolones (e.g., ciprofloxacin), or ampicillin if in vitro susceptibility has been proven.

Intestinal ischemia

Endovascular revascularization is the preferred treatment for hemodynamically stable patients with acute mesenteric ischemia who do not present with signs or symptoms of advanced intestinal ischemia (e.g., peritonitis, sepsis). This procedure is minimally invasive, and studies suggest similar efficacy to open surgical treatment. Reassuring vital signs and benign abdominal examination findings in this patient suggest acute bowel ischemia without permanent infarction, which is likely to resolve with the restoration of blood flow. This patient should also receive supportive measures (e.g., intravenous fluids, nasogastric decompression, broad-spectrum antibiotics) as well as anticoagulation, preferably with unfractionated heparin.

Lipid disorders

This patient presents with xanthelasmas, small nodular lipid deposits that manifest bilaterally on the upper eyelids. Xanthelasmas are a symptom of underlying lipid disorders (e.g., familial hypercholesterolemia, obesity), which increase the risk for atherosclerosis and associated cardiovascular diseases such as coronary artery disease, myocardial infarction, and stroke. The next best step in management would be to identify the underlying cause of this patient's lipid disorder via laboratory analysis of serum lipid levels.

Lipid-lowering agents

Niacin upregulates prostaglandin synthesis in the skin by activating a G-protein coupled receptor in keratinocytes and dermal Langerhans cells. These prostaglandins cause cutaneous flushing, which is sometimes accompanied by paresthesias such as tingling or itching. The flushing typically begins within an hour of niacin intake. NSAIDs (e.g., aspirin, ibuprofen) taken 30–60 minutes before niacin can prevent flushing by inhibiting prostaglandin synthesis. Alternatively, the use of an extended-release niacin formulation, which is associated with less flushing, can be considered. Niacin-induced flushing often subsides over the course of a few weeks as a result of tachyphylaxis.

After discontinuation of simvastatin for a period of 2–4 weeks and once symptoms have resolved, the patient should begin treatment with low-dose pravastatin (or fluvastatin). These statins have been shown to have the lowest risk of muscular side effects. If symptoms of myopathy do not occur, the dose can be adjusted to achieve the goals outlined in the guidelines for lipid-lowering therapy.

Elevated transaminases occur in up to 3% of patients receiving statin therapy. This asymptomatic side effect typically resolves spontaneously over time. However, in very rare cases, overt hepatotoxicity can occur, resulting in transaminitis (> 10 times the upper normal limit of transaminases).

Long QT syndrome

Beta blockers such as propranolol are the mainstay of therapy for congenital LQTS. Patients with symptomatic LQTS (history of syncope or cardiac arrest) should be treated with beta blockers to reduce the risk of polymorphic ventricular tachycardia and sudden cardiac death. Left cardiac sympathetic denervation (stellectomy) should be considered in patients not responsive to beta blockers. In high-risk patients (recurrent syncope despite medical therapy, survival of cardiac arrest) an implantable cardioverter defibrillator is indicated. There are multiple variants of LQTS that can manifest with associated conditions, including congenital deafness. The absence of sensorineural hearing loss in this patient suggests Romano-Ward syndrome rather than Jervell and Lange-Nielsen syndrome.

Mitral regurgitation

Chronic MR leads to chronic volume overload of the left ventricle (LV) (normal stroke volume + regurgitated volume), which triggers eccentric hypertrophy of the left atrium and ventricle to compensate for the overload and maintain the cardiac output. Decompensation of chronic MR due to progressive LV dilation and myocardial dysfunction results in decreased stroke volume (↓ cardiac output), increased left ventricular end-diastolic pressure (due to↑ end-systolic and end-diastolic volume), and increased pulmonary artery pressure (blood backs up into pulmonary veins and ultimately pulmonary artery). Because chronic MR leads to LV hypertrophy, ECG changes can include deviation of the ST segment in the opposite direction of the QRS complex (discordance) and T-wave inversions. Further features of chronic MR include palpitations (due to conduction abnormalities, e.g., atrial fibrillation) and an early-diastolic heart sound (S3 is a sign of diastolic ventricular volume overload).

Papillary muscle rupture, a life-threatening early complication of myocardial infarction (MI), typically develops within 2–7 days of MI and may cause acute MR. In addition to clinical features of acute left-sided HF and a systolic murmur, findings may also include a midsystolic click due to mitral valve prolapse. ECG findings are unspecific and may show T-wave inversion as a sign of previous and/or current cardiac ischemia. Papillary muscle rupture is more common in patients with involvement of the right coronary, which supplies the posteromedial papillary muscle through the posterior descending artery without any collateral blood supply. The diagnosis can be confirmed using echocardiography, which often shows flailing of a valve segment. The treatment of choice is surgical repair.

This patient's auscultatory findings indicate chronic mitral regurgitation (MR) as the cause of his LHF. MR typically manifests with a high-frequency, holosystolic blowing murmur that radiates into the axilla and is heard best at the apex. Mitral murmurs are heard best during expiration and while the patient lies on the left side. Causes of primary MR include degenerative mitral valve disease (mitral valve prolapse, mitral annular calcification, ruptured chordae tendineae), infective endocarditis, and rheumatic fever.

Mitral Stenosis

Percutaneous mitral balloon commissurotomy (PMBC) is the treatment of choice for many cases of symptomatic mitral stenosis because it improves valve function and symptoms, is less invasive, and the morbidity and mortality rates are lower than with other surgical treatment options. This patient has a favorable valve morphology (no calcifications) and no evidence of a left atrial thrombus or mitral regurgitation, which makes him a good candidate for PMBC. If the patient's echocardiography were less benign, open valvular replacement would be indicated.

Long-standing mitral stenosis can lead to an enlarged left atrium due to chronically elevated left atrial pressures. In some patients, the atrium may become so massively enlarged that it can compress the esophagus. In only very rare cases do patients develop esophageal compression that is severe enough to cause dysphagia (dysphagia megalatriensis). Other rare complications associated with massive enlargement of the left atrium include recurrent laryngeal nerve palsy (Ortner syndrome) and massive hemoptysis due to erosion of the bronchial arteries.

This patient's diastolic murmur (audible after S2) at the fifth left intercostal space and opening snap indicate mitral valve stenosis, which causes an increase in left atrial pressure (and increased pulmonary wedge pressure) and a backup of blood into the lungs. Volume overload eventually causes symptoms of cardiogenic pulmonary edema, which explains this patient's orthopnea, hemoptysis, and crackles. The absence of P waves confirms atrial fibrillation, a common complication of mitral stenosis. This patient most likely suffered from rheumatic fever, the most common cause of mitral stenosis.

Mitral valve prolapse

Myxomatous degeneration is caused by the accumulation of dermatan sulfate within the connective tissue of the mitral valve. In developed countries, it is the most common cause of mitral valve degeneration and subsequent mitral valve prolapse. As the disease course progresses, mitral regurgitation can occur. This patient presents with common features of mitral valve prolapse (palpitations, anxiety, chest pain, mid-systolic click). The new-onset dyspnea, holosystolic murmur, and crackles on lung auscultation are consistent with regurgitation of the mitral valve, indicating an advanced disease process.

Myocardial infarction

This patient's persistent retrosternal chest pain with ST-segment elevation on ECG in leads I, aVL, and V1–V4 are all consistent with an ST-segment elevation myocardial infarction (STEMI) caused by an occlusion of the proximal left anterior descending artery (LAD). Acute occlusion of the proximal LAD leads to infarction of the anterior wall of the left ventricle. Reciprocal ST-segment depressions may be seen in the inferior leads; this patient's ECG shows reciprocal ST-segment depressions in II, III and aVF. ST elevations typically develop in leads V1–V6 on ECG as a result of infarcts that involve the proximal LAD. Leads V1–V2 correspond to the anteroseptal territory; leads V3–V4 correspond to the anteroapical territory; leads V5–V6 correspond to the anterolateral territory. In some cases, ST elevations in the lateral leads (leads I and aVL) can also develop.

Postmyocardial infarction syndrome (Dressler syndrome), a type of postcardiac injury syndrome, usually occurs 2–10 weeks after MI due to immune-complex mediated damage (type III hypersensitivity reaction) in the pericardium. The exact mechanism of immune-complex formation in Dressler syndrome is not completely understood, but the release of neo-antigens from the infarcted myocardium is suspected to play a role. Patients typically present with features of acute pericarditis such as fever, tachypnea, chest pain that is worse during inspiration and relieved by leaning forward, a dry cough (due to inflammation of the mediastinal pleura adjoining the pericardium), a pericardial rub, increased troponin levels, and diffuse ST elevations on ECG. Dressler syndrome may also cause pericardial effusion. Dressler syndrome is treated with NSAIDs, preferably high-dose aspirin.

Long-term dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 receptor inhibitor (e.g., clopidogrel, prasugrel, ticagrelor) is the recommended regimen for all patients after reperfusion therapy. DAPT reduces mortality and the risk of developing subsequent ischemic episodes and stent thrombosis. The duration of DAPT is an individual decision based on bleeding risk and the risk of stent thrombosis. After PCI with stent placement, DAPT is usually recommended for 12 months. In addition to DAPT, long-term pharmacotherapy for secondary prevention after acute coronary syndrome consists of an ACE inhibitor, beta blocker, nitrate, and high-dose statin therapy. Low-dose aspirin therapy is continued lifelong.

Occlusion of the proximal right coronary artery (RCA) can cause an inferior wall myocardial infarction, which in turn can present atypically with epigastric pain. High-degree atrioventricular block can occur in this setting because the sinoatrial node (SA node) and atrioventricular node (AV node) are usually supplied by the RCA (the SA node directly, and the AV node via the AV nodal branch). Right-sided leads (V4R, V5R, and V6R) should also be obtained to evaluate for right ventricular (RV) infarction (especially given the patient's jugular venous distention), as the RCA supplies the RV via its right marginal branch.

Interventricular septum rupture typically occurs 3–5 days after myocardial infarction. It manifests with sudden onset hemodynamic instability (hypotension, tachycardia, tachypnea) and signs of right ventricular failure (jugular venous distention, parasternal heave, pedal edema, and characteristically clear lungs) due to the development of a left-to-right shunt. This patient's new-onset holosystolic murmur is the result of blood flow across the newly formed ventricular septal defect (analogous to the classic murmur of a ventricular septal defect).

NSAIDs are the first-line treatment for Dressler syndrome because they provide pain relief and have antiinflammatory properties. Aspirin is usually preferred over other NSAIDs because it is indicated for secondary prophylaxis after an acute MI. Combining aspirin with another NSAID increases the risk of gastrointestinal bleeding and kidney injury. The higher dosage of aspirin is maintained until symptoms resolve (usually 3–4 weeks), then tapered to the standard prophylaxis dosage. Rare complications of Dressler syndrome include pericardial effusion, pericardial tamponade, and constrictive pericarditis. Dressler syndrome is an autoimmune response to cardiac muscle cells that occurs > 1 week after MI. This process is distinct from acute post-MI pericarditis, which occurs within 1 week of the event and is caused by an infarction located very close to the pericardium that causes direct irritation. The treatment of post-MI pericarditis is usually supportive; NSAIDs (except for aspirin) should be avoided for 7–10 days after an acute MI.

Ventricular aneurysms can develop several weeks to months after an MI because of scar tissue formation that leads to thinning and weakening of the ventricular wall. This in turn can lead to congestive heart failure, which is a common complication of ventricular aneurysms. Other complications of ventricular aneurysms include myocardial wall rupture (which can lead to cardiac tamponade), arrhythmias, and mural thrombus formation within the aneurysmal segment (due to stasis of blood flow). Ventricular aneurysms typically manifest with a systolic murmur, an S3 and/or S4 gallop, and persistent ST elevations on ECG, all of which are seen here. Diagnosis is confirmed by visualization of the pathological myocardial wall protrusion on echocardiography.

Mural thromboembolism from a left ventricular pseudoaneurysm is the most likely cause of this patient's acute limb ischemia. A left ventricular pseudoaneurysm typically develops 3–14 days after myocardial infarction, and it can also lead to decreased cardiac output and arrhythmia. Initial diagnosis of a ventricular pseudoaneurysm is performed with transthoracic echocardiography, but a definitive diagnosis is determined with angiography, which allows direct visualization of the lesion. Mural thromboembolism can also be associated with a true ventricular aneurysm. As true ventricular aneurysm typically develops 2 weeks to a few months postinfarction, this patient is more likely to have a ventricular pseudoaneurysm.

This patient with ST-segment elevation on ECG and elevated troponin T was correctly started on unfractionated heparin, dual antiplatelet therapy (aspirin and ticagrelor), and sublingual nitroglycerin for his ST-segment elevation MI (STEMI). He would also benefit from early initiation of a high-dose statin such as atorvastatin. This intervention has been shown to improve long-term outcomes regardless of baseline LDL and cholesterol levels. Patients with STEMI should undergo emergency coronary angiography with percutaneous coronary intervention (PCI); ideally, door-to-PCI time should be < 90 minutes but not exceed 120 minutes. Thrombolytic therapy is indicated if PCI cannot be performed ≤ 120 minutes after first medical contact or if PCI was unsuccessful.

Acute inferior myocardial infarction (MI) is the most likely diagnosis in a patient with dyspnea, lightheadedness, ST elevation in the inferior leads (II, III, aVF), and reciprocal ST depression in leads I and aVL. This patient has significant risk factors for atherosclerotic disease, including type 2 diabetes mellitus and a 20 pack-year smoking history. Acute STEMI is usually diagnosed based on the initial ECG and the presence of typical ischemic chest pain. However, diabetic patients and elderly women may have an atypical presentation with little or no chest pain and predominantly autonomic symptoms (e.g., nausea).

Sudden cardiac death after MI is usually due to ventricular tachyarrhythmias such as ventricular tachycardia or ventricular fibrillation. These ventricular arrhythmias result in dysfunctional ventricular contraction, which compromises cardiac output and ultimately leads to asystole. Patients with ventricular fibrillation require rapid defibrillation and cardiopulmonary resuscitation, otherwise hemodynamic instability can lead to loss of consciousness and SCD, which is the leading cause of death post-MI.

Myocarditis

Myocarditis has a wide range of clinical presentations, from subclinical (and often undiagnosed) myocarditis to dilated cardiomyopathy with features of acute decompensated heart failure, as seen in this patient. Myocarditis is most commonly caused by viral infections and most often affects young adults. If myocarditis is suspected, an ECG, cardiac biomarkers (e.g., troponin), and chest x-ray should be obtained. ECG may show nonspecific signs of myocardial damage (e.g., T-wave inversions, tachycardia); cardiac biomarkers and inflammatory markers (e.g., ESR) are typically elevated. Echocardiography is indicated to evaluate ventricular dysfunction. In patients with myocarditis complicated by dilated cardiomyopathy, echocardiography typically shows ventricular dilation and global ventricular hypokinesis.

Myocarditis is most commonly caused by viral infections (e.g., Coxsackie B virus infection, parvovirus B19 infection, HHV-6 infection) and Coxsackie B virus is the most common cause of viral myocarditis in children and adolescents. Features of cardiac dysfunction may be preceded by signs of infection (e.g., flu-like symptoms, gastrointestinal symptoms). In children, myocarditis is rare and symptoms are often more severe than in adults, who typically have mild or even no symptoms. Children are also more often affected by complications (e.g., cardiac arrhythmias, cardiogenic shock) than adults and require careful management (e.g., cardiorespiratory monitoring, management of heart failure with diuretics). Further management of this patient would include an ECG and echocardiography to assess the severity of cardiac dysfunction.

Major depressive disorder

This patient meets the diagnostic criteria for a major depressive episode. Depression post-myocardial infarction is an independent risk factor for subsequent cardiovascular events and doubles the risk of short and long-term all-cause mortality. Poor prognosis is mainly due to reduced adherence to medications and diminished engagement in healthy behaviors (e.g., participation in a cardiac rehabilitation program). All patients with cardiovascular disease should undergo screening for depression, e.g., with screening tools like the PHQ-2 or PHQ-9. Effective treatment for depression with SSRIs and psychotherapy improves prognosis.

Nitrates

Development of nitrate tolerance leading to decreased drug effectiveness is a typical side effect of long-term therapy. The underlying mechanism is not completely understood but is thought to involve decreased sensitivity of the vascular endothelium to nitrates. The most effective strategy to prevent nitrate tolerance is intermittent therapy with nitrate-free intervals of at least 8 hours, which would be accomplished by avoiding isosorbide dinitrate at night.

Nitrates, such as nitroglycerin, cause arterial and venous vasodilation by inducing smooth muscle relaxation. Anginal pain relief is mainly achieved by venous dilation (venous pooling), which leads to decreased end-diastolic pressure (i.e., decreased preload), reduced myocardial wall tension, and improved myocardial perfusion. The decreased preload results in reduced heart size and decreased myocardial oxygen demand. To a lesser degree, nitrates decrease afterload by triggering arterial vasodilation, thus reducing myocardial contraction effort and oxygen demand. Because the coronary arteries are already fully dilated in patients with CAD in an attempt to provide as much oxygen to cardiac tissue as possible, the effect of nitrates on these vessels is limited. Life-threatening hypotension may occur if nitrates are taken within 24 hours of a PDE-5 inhibitor such as sildenafil.

Nonthrombotic embolism

Venous air embolism develops when air enters the venous circulation. This can occur during neurosurgical procedures, especially those that require the patient to be in a sitting position. In this position, the negative (subatmospheric) pressure of the cranial veins due to them being at a higher level than the heart can result in air being sucked into the cranial veins. Other causes of venous air embolism include vascular interventions (e.g., insertion or removal of central venous catheters), penetrating lung injuries, and barotrauma. Management procedures depend on the suspected site of embolism and include compression of the suspected entry site, correction of hypoxia and hypotension, and placing the patient in a head-down position (e.g., Trendelenburg position) or in the left lateral decubitus position (Durant maneuver), both of which help trap the air emboli in the right ventricular apex and therefore prevent further obstruction of the pulmonary outflow tract. If the patient remains unstable following these procedures, direct aspiration of air through a central venous catheter may be considered.

Obstructive sleep apnea

The collapse of pharyngeal muscles during sleep leading to transient nocturnal upper airway obstruction is the main mechanism underlying obstructive sleep apnea (OSA). Typical features of this disease include nocturnal snoring, morning headaches, poor concentration, daytime sleepiness, fatigue, and depression. Nocturnal apneic episodes in individuals with OSA result in nocturnal hypercapnia, which, in turn, causes an increased sympathetic response that leads to secondary hypertension. Obesity, especially around the neck, is the most important risk factor for developing OSA, and weight loss will often improve symptoms.

Pharmacology

Proton pump inhibitors (PPIs) are metabolized by a specific class of cytochrome-P450 enzymes but can also function as inhibitors of this enzyme class (substrate inhibition). This results in a vicious cycle of increasing serum PPI levels and at high concentrations, certain PPIs such as omeprazole and esomeprazole can inhibit the class of cytochrome-P450 enzymes that metabolize the pharmacologically active stereoisomer of warfarin. Through cytochrome-P450 inhibition, these PPIs can increase warfarin concentration to supratherapeutic levels and precipitate warfarin toxicity. Other drugs that can precipitate warfarin toxicity through cytochrome-P450 inhibition include amiodarone (an antiarrhythmic), sodium valproate (an antiepileptic), azole antifungals, and certain antibiotics (e.g., metronidazole, sulfonamides, chloramphenicol).

Pericarditis

This patient's history of breast radiation therapy, shortness of breath, nonproductive cough, and sharp substernal chest pain that worsens in the supine position make acute radiation-induced pericarditis the most likely diagnosis. This diagnosis is further supported by her friction rub (triphasic scratching sound) and ECG showing diffuse ST segment elevation. Pericardial involvement is a common adverse effect of radiation therapy of the chest. In the acute setting, exposure to high doses of radiation causes cellular injury, which leads to the release of inflammatory mediators and cytokines, resulting in neutrophilic infiltration of the pericardium. Several years after radiation therapy, individuals may develop constrictive pericarditis, which is characterized by fibrotic thickening of the pericardium and manifests with symptoms of fluid overload. Other long-term cardiovascular adverse effects of radiation therapy include cardiomyopathy, valvular heart disease, coronary artery disease, and conduction abnormalities.

Pericarditis is a common cause of cardiac tamponade; it may occur in cases in which the pericardium becomes scarred and less elastic, while increased amounts of inflammatory fluids are secreted into the pericardial space. Cardiac tamponade can lead to hemodynamic compromise; therefore, treatment with pericardiocentesis is indicated. Another complication of acute pericarditis is chronic, constrictive pericarditis, which may develop after several years.

The most common causes of acute pericarditis are 1.) idiopathic (assumed viral etiology), followed by 2.) cases of confirmed viral etiology. The most common causes of viral pericarditis are coxsackievirus B and echovirus; other pathogens include hepatitis viruses, influenza virus, measles virus, mumps virus, varicella virus, and HIV. Idiopathic cases are presumed to be viral because efforts to confirm etiology are not routinely pursued due to the expenses involved, the inaccessibility of pericardial tissue/fluid, and the time delay and inaccuracy of viral studies (e.g., culture, PCR, viral serology). In most cases, clinical management is not changed by these results.

Antiinflammatory therapy to control pain and prevent recurrence is the mainstay of management in patients with acute pericarditis because this condition is most often self-limited. While NSAID therapy (e.g., with ibuprofen) usually provides symptomatic relief, it is often used in combination with colchicine, which improves response to therapy and reduces recurrence rates. In patients with nonviral underlying causes (e.g., bacterial, autoimmune, uremic), specific therapy is also indicated; this patient's history of recent upper respiratory tract infection suggests a viral etiology and, therefore, no other specific treatment is needed. Patients should restrict physical activity until symptoms have resolved and C-reactive protein has normalized; for athletes, ECG and echocardiogram findings should also be normal before training is resumed. Treatment with glucocorticoids may also be considered in patients with contraindications to NSAIDs and patients in whom treatment with NSAIDs and colchicine has been unsuccessful. Glucocorticoid treatment is also indicated in patients with pericarditis resulting from autoimmune disease.

Pericardiectomy, along with the treatment of any underlying condition (i.e., this patient's tuberculosis), is the recommended approach for constrictive pericarditis. In constrictive pericarditis, a thick, rigid, and fibrous pericardium compromises cardiac function, which is restored by the removal of the fibrotic pericardium. In patients without signs of chronic constrictive pericarditis (i.e., no pericardial calcifications, atrial fibrillation, hepatic dysfunction, anasarca, or cachexia), pharmacotherapy can be attempted first. This can include NSAIDs, colchicine, diuretics, corticosteroids, and immunomodulatory therapy; these measures should also be considered as adjuncts to pericardiectomy in chronic constrictive pericarditis. In healthy individuals, the velocity of blood flow in the left side of the heart normally decreases with inspiration. However, in patients with constrictive pericarditis, this decrease in blood flow is exaggerated (> 25% decrease in diastolic flow across the mitral valve) because the rigid, fibrotic, shell-like pericardium impedes diastolic

filling due to impaired relaxation of the left ventricle. In addition to these findings, an echocardiogram would show acoustic shadowing (caused by calcifications) and thickening of the pericardium.

This patient's acute chest pain and dyspnea in combination with the ECG findings are suggestive of acute pericarditis. This condition is most commonly caused by a viral infection, indicated by the fever, runny nose, and dry cough this patient had 1 week ago. Acute pericarditis typically manifests with acute sharp retrosternal pain that is exacerbated by inspiration and coughing and improves with sitting and leaning forward. However, patients may present with atypical chest pain, as seen in this case. For the diagnosis of acute pericarditis, at least two of the following four criteria must be present: a characteristic chest pain (pleuritic), a pericardial friction rub, typical ECG changes (diffuse, concave-upward ST segment elevations), and new or worsening pericardial effusion on echocardiography. A pericardial high-pitched friction rub on auscultation is present in 85% of patients with acute pericarditis and, in combination with this patient's ECG findings, would confirm the diagnosis.

Diffuse, concave ST segment elevations in multiple leads are the typical ECG findings seen in patients with acute pericarditis. The ST segment elevations are typically present in all leads except for aVR and V1, which may show ST segment depressions. ECG may also show diffuse PR segment depressions. Though the most common cause of pericarditis is viral infection, the most likely etiology in this patient is her underlying diagnosis of rheumatoid arthritis. Management of nonbacterial pericarditis includes administration of NSAIDs and, in severe cases, glucocorticoids. In contrast to the diffuse, concave ST segment elevations of pericarditis, ST segment elevations in ST segment elevation myocardial infarction typically have a convex morphology and are present in the leads that correspond to the perfusion territory of a specific coronary artery.

Normally, the decrease in intrathoracic pressure during inspiration expands the compliant right ventricle, resulting in a decrease in jugular venous pressure. In constrictive pericarditis, compliance of the right ventricle is decreased and the right ventricle fails to expand during inspiration. This, alongside a possible increase in baseline jugular venous pressure in constrictive pericarditis due to restricted right ventricular filling during late diastole, leads to an increase in jugular venous pressure during inspiration, and therefore, jugular venous distention on inspiration. This phenomenon, which is called Kussmaul sign, can also be seen in patients with restrictive cardiomyopathy and right atrial or ventricular tumors. Management options for constrictive pericarditis include NSAIDs, colchicine, glucocorticoids, pericardiectomy, and treatment of the underlying condition (e.g., antitubercular or immunomodulatory therapy). In cardiac tamponade without underlying pericarditis (e.g., traumatic hemopericardium), the jugular venous pressure is increased as a result of impaired right ventricular filling. However, the right ventricle is still compliant and a

decrease in intrathoracic pressure can be transmitted to the right ventricle across the fluid-filled pericardial sac. Kussmaul sign would not be expected in traumatic cardiac tamponade.

Purulent pericarditis most commonly develops after thoracic surgery or cardiac injury and is typically caused by Staphylococcus spp., Streptococcus spp., or (where it is endemic) Mycobacterium tuberculosis. The diagnosis is typically confirmed based on the presence of purulent exudate in the pericardial sac on echocardiography. Immediate management consists of pericardiocentesis to rapidly resolve pericardial effusion and/or cardiac tamponade. Subsequently, pericardial fluid and blood cultures should be conducted, followed by empiric intravenous antibiotic therapy (e.g., vancomycin, ceftriaxone, or meropenem), then targeted antibiotic therapy based on culture results. Surgical drainage or intrapericardial fibrinolysis may be necessary if there is loculation.

A pericardial knock is a high-pitched, early-diastolic sound that sounds like a premature S3. A pericardial knock is often heard on auscultation in constrictive pericarditis due to the abrupt halting of diastolic ventricular relaxation and filling by the rigid pericardial sac. In constrictive pericarditis, reduced ventricular filling leads to manifestations of reduced cardiac output (forward failure), such as fatigue and/or dyspnea, as well as those of fluid overload (backward failure), such as jugular venous distention, positive Kussmaul sign, hepatomegaly, and the clinical features seen in this patient.

While tuberculosis is the most likely underlying cause of constrictive pericarditis in this patient, other etiologies include prior cardiac surgery, radiation therapy to the chest, viral infection, and connective tissue diseases.

Pulmonary embolism

PE is usually preceded by deep vein thrombosis (DVT), which in the vast majority of cases (≥ 90%) occurs in the iliac vein and other proximal deep veins of the lower extremities (e.g., femoral and popliteal vein). Over 50% of patients with thrombosis in the iliac, femoral, or popliteal veins also go on to develop PE. When a patient presents with PE, it is important to examine for signs of DVT (e.g., physical examination, venous compression ultrasonography). Typical ECG findings of PE include sinus tachycardia and signs of right ventricular pressure overload, such as right bundle branch block, T-wave inversion in the precordial leads and/or inferior leads, an SIQIIITIII-pattern, and right axis deviation.

Hemodynamically stable patients (systolic blood pressure > 90 mm Hg) with a high clinical probability of PE and no contraindications for anticoagulation should be started on empiric anticoagulation even before the diagnosis is confirmed. Low molecular weight heparin (LMWH) is the treatment of choice for venous thromboembolism (including PE) unless the patient has poor kidney function (e.g., CrCl < 30 mL/min) or requires quick reversal of anticoagulation (e.g., impending therapy with thrombolysis or embolectomy, or surgery). This patient has laboratory values indicating normal kidney function and she currently has no indications for therapy with thrombolysis or embolectomy, e.g., right heart failure or the need for resuscitation. Therefore, empiric anticoagulation with LMWH should be initiated before pursuing a definitive diagnosis. Once the diagnosis is confirmed, the next step is to assess the patient's overall mortality risk and early outcome using the pulmonary embolism severity index (PESI, sPESI). Outpatient management may be considered in patients who have a low 30-day mortality risk (PESI classes I and II).

Pericardial effusion and cardiac tamponade

Creating a pericardial window is the most appropriate treatment for this hemodynamically stable patient with recurrent pericardial effusion. In this surgical procedure, part of the pericardium is removed to continuously drain excess fluid from the pericardial space into the pleural cavity, providing pericardial decompression. Pericardial window is often indicated in recurrent malignant pericardial effusion because it prevents the reaccumulation of fluid and, therefore, offers definitive treatment.

Transthoracic echocardiography is a quick, inexpensive, side-effect-free, and reliable method for detecting pericardial effusion and cardiac tamponade. This imaging technique typically shows an anechoic space between the pericardium and epicardium, indicating fluid accumulation. In a hemodynamically unstable patient like this one, an eFAST examination in the trauma bay is likely to reveal effusion; transthoracic echocardiography is used to evaluate the size and hemodynamic effect of the effusion and determine the best approach for draining the effusion. In patients with hemodynamic instability and evidence of cardiac tamponade on echocardiography, urgent pericardial fluid drainage (e.g., ultrasound-guided pericardiocentesis) is indicated.

In cardiac tamponade, outward expansion of the ventricles is limited because of fluid in the pericardial space. During inspiration, increased venous return leads to increased right ventricular volume. As outward expansion is limited, the right ventricle expands via the interventricular septum, which bulges into the left ventricle. This effect leads to further reduction in left ventricular filling during inspiration, resulting in decreased stroke volume and a subsequent drop in blood pressure. A drop in systolic blood pressure > 10 mm Hg during inspiration is known as pulsus paradoxus, a sign characteristically seen in moderate and severe cardiac tamponade but also in some cases of severe asthma, tension pneumothorax, and constrictive pericarditis.

Postpericardiotomy syndrome typically manifests 1–6 weeks after cardiothoracic surgery as a result of an autoimmune inflammatory process in the pericardium. This syndrome may be accompanied by pericardial effusion, which can lead to cardiac tamponade, manifesting with muffled heart sounds and pulsus paradoxus. Fluid accumulation in the pericardial space leads to compression of the heart (especially the right ventricle because of its thin wall). This compression results in a shift of the interventricular septum toward the left ventricle and impaired left ventricular diastolic filling (decreased preload). Cardiac output subsequently decreases and symptoms of backward heart failure (e.g., peripheral edema and jugular venous distension due to right-sided heart failure) and forward heart failure (e.g., progressive fatigue) develop. Pericardial effusion causing cardiac tamponade is a life-threatening condition that requires drainage of the pericardial fluid (e.g., using pericardiocentesis).

Severe pericardial effusion and subsequent cardiac tamponade are life-threatening conditions that require immediate decompression with pericardiocentesis. Pericardiocentesis is indicated for hemodynamic stabilization and symptom relief before treatment of the underlying condition (e.g., with hemodialysis) can be started. This patient with diabetes has a history of chronic kidney disease (CKD), likely as a result of inadequately managed hyperglycemia. CKD leads to elevation of both serum creatinine and BUN, which can result in chronic pericardial effusion due to uremia. The patient's anemia (due to decreased EPO levels) and bilateral crackles indicating pulmonary edema (due to fluid retention) also likely result from CKD. In hemodynamically stable patients with pericardial effusion, the underlying cause should be treated first. If an effusion is due to underlying malignancy, a pericardial window is performed to continuously drain the fluid.

Preceded by an episode of flu-like symptoms, this patient's history of chest pain that increases with respiration and decreases while sitting up is suggestive of acute pericarditis. This patient most likely has cardiac tamponade as a complication of acute pericarditis. Cardiac tamponade can occur if increased amounts of inflammatory fluid are secreted into the pericardial space, compressing the cardiac chambers. This leads to decreased ventricular diastolic filling and decreased cardiac output. Other common causes of cardiac tamponade include aortic dissection and chest trauma. Hemodynamically unstable patients should be treated with ultrasound-guided pericardiocentesis or surgical drainage in order to decompress the pericardium.

Electrical alternans is an ECG finding that is highly specific to large pericardial effusions. This finding is characterized by cyclical changes (alterations) in the axis or amplitude of consecutive QRS complexes, which can be attributed to the swinging motion of the beating heart surrounded by pericardial fluid. In addition, ECG in patients with large pericardial effusion and cardiac tamponade typically shows sinus tachycardia and low voltage recording. Management of pericardial effusion depends on the patient's hemodynamic stability: In stable patients, transthoracic echocardiography should be used to confirm the diagnosis. In unstable patients and those in cardiac arrest with suspected tamponade, pericardiocentesis should not be delayed for diagnostic confirmation.

Peripheral arterial disease

Ankle-brachial index (ABI) is the first-line diagnostic test in PAD because it is readily available, noninvasive, as well as highly specific and sensitive. Reduced ABI values between 0.4–0.9 indicate mild to moderate PAD with claudication, whereas values below 0.4 correlate to severe PAD with resting pain and/or gangrene. An ABI > 1.4 in patients with suspected PAD may indicate calcific sclerosis with noncompressible vascular walls (e.g., in patients with diabetes). A low ABI (≤ 0.9) and a high ABI (> 1.4) are associated with an increased risk of all-cause and cardiovascular mortality. In patients with a normal ABI and high suspicion for PAD, exercise testing may be required. Vascular imaging (e.g., with MR angiography) is not required for diagnosis but helps assess site(s) and extent of arterial occlusion or stenosis and collateral blood flow if revascularization is planned.

Decreased pulses are a common finding in peripheral arterial disease, for which this patient is at high risk. Decreased bilateral femoral pulses indicate occlusion of either the bilateral iliac arteries or the aortic bifurcation. Lesions at either of these locations cause aortoiliac occlusive disease (Leriche syndrome), which manifests with the classic triad of buttock, hip, or thigh claudication; erectile dysfunction; and absent or diminished femoral pulses. Given this patient's high risk for cardiovascular disease and complaints in accordance with two-thirds of the classic triad, Leriche syndrome is the most likely diagnosis. Atrophy of the affected limbs is also common in Leriche syndrome.

PAD is a very strong predictor of coexisting coronary artery disease, as both diseases have a similar pathogenesis (atherosclerosis) and shared risk factors (e.g., smoking, hypertension, hyperlipidemia, diabetes). Compared to healthy individuals, patients with PAD are at significantly increased risk for myocardial infarction and stroke. Evaluation and management of underlying coronary artery disease is recommended for patients with PAD, and risk factors should be addressed. First-line therapy of lower extremity PAD is management of cardiovascular risk factors (e.g., smoking, diabetes, hypertension) and exercise (walking) therapy.

Cilostazol is a phosphodiesterase III inhibitor that has vasodilatory, antiplatelet, and antithrombotic properties. This drug may be considered as a therapeutic trial for 3–6 months in patients with PAD and claudication who remain symptomatic despite conservative measures (e.g., smoking cessation, supervised exercise therapy). Cilostazol improves symptoms of claudication and walking distance but has not been shown to decrease major cardiovascular events. Adverse effects are common and include headache, palpitations, diarrhea, and dizziness. In addition to cilostazol, all patients with PAD should receive medical therapy with an antiplatelet agent (aspirin or clopidogrel), a statin to reduce the risk of myocardial infarction, stroke, and mortality, and antidiabetic agents if appropriate.

Intensive treatment and optimization of risk factors for atherosclerotic disease improve outcomes in PAD and prevent ischemic events. Statins help to control hyperlipidemia and should be offered to all patients with PAD. Antiplatelet therapy (e.g., with clopidogrel) is indicated in all symptomatic patients. Other cardiovascular risk factors that require long-term treatment are hypertension (controlled with enalapril in this patient) and hyperglycemia. A thorough workup of this patient is warranted, as PAD often coexists with coronary artery disease, stroke, atrial fibrillation, and renal disease.

Conservative interventions, such as structured exercise therapy, are the best initial steps in the management of PAD if claudication is present and there is no evidence of chronic limb-threatening ischemia or acute limb ischemia. Initial management would also include modifying risk factors through smoking cessation, antiplatelet therapy, statin therapy, and managing hypertension and diabetes mellitus if present.

In patients with CLTI, urgent revascularization therapy is indicated to prevent limb-threatening arterial occlusion. Revascularization can be performed via percutaneous transluminal angioplasty or bypass surgery, depending on the extension and location of the stenotic/occluded segment. In patients with extensive disease manifesting with long-segment and/or multifocal stenoses or occlusions, as seen here, femorotibial bypass surgery is preferred over endovascular revascularization, as long-term patency rates are higher. This patient also has dry gangrene. After successful revascularization, amputation of unsalvageable regions may be performed (staged procedure).

This patient's symptoms of arterial insufficiency (paresthesia, intermittent claudication) in his right calf and foot and palpable femoral pulses but absent right pedal pulses indicate stenosis of the femoropopliteal artery, the most common site of peripheral arterial disease. The foot tingling on leg elevation is due to the decrease in arterial blood flow to the limb when raised above the level of the heart (usually insignificant, but can cause symptoms in patients with preexisting arterial insufficiency). The cramping pain upon exertion (e.g., walking on the treadmill) and relief at rest are characteristic of intermittent claudication (stage II according to Fontaine classification), which is a symptom of arterial insufficiency. Chronic smoking, hypertension, advanced age, and male gender are all significant risk factors for the development of PAD.

Pulmonary hypertension and cor pulmonale

Chronic pulmonary hypertension (PH) leading to cor pulmonale is the most likely cause of this patient's RHF. This patient with a history of heavy smoking presents with chronic cough and dyspnea, diffuse expiratory wheezes, and pulmonary hyperinflation (distant heart sounds), which indicates chronic obstructive pulmonary disease (COPD). COPD causes chronic hypoxic pulmonary vasoconstriction which progresses to irreversible remodeling of the walls of the pulmonary arteries, resulting in group 3 PH. In a patient with COPD, a right ventricular strain pattern on ECG or worsening dyspnea or exercise intolerance with stable spirometry findings raise suspicion for PH. If PH is left untreated, the chronically elevated right ventricular afterload eventually causes reduced right-sided cardiac output (i.e., RHF). Reduced output of the right heart leads to elevated central venous pressure and systemic venous congestion, resulting in fluid accumulation in various tissues (e.g., liver, kidneys, peripheral tissue). Elevated central venous pressure also impairs lymphatic drainage, contributing to fluid retention. If clinical suspicion is high for PH, perform transthoracic echocardiography (TTE) to noninvasively identify markers of elevated pulmonary artery pressure. Right heart catheterization is the confirmatory test for pulmonary hypertension. The causes of PH are classified into five groups: (1) idiopathic or hereditary, (2) left-sided heart disease, (3) chronic hypoxic lung disease, (4) chronic thromboembolism, and (5) unclear multifactorial mechanisms.

Mitral stenosis leads to increased left atrial pressure, causing both left atrial dilatation, which may result in atrial fibrillation, and an increase in pulmonary arterial pressure to overcome the increased left heart pressure (pulmonary hypertension). Over time, this will lead to pulmonary vascular remodeling, increased pulmonary vascular resistance, splitting of S2, and right ventricular hypertrophy (as indicated by the right axis deviation) to compensate. Right ventricular failure eventually manifests with characteristic features such as jugular venous distention and pitting edema.

Right-heart catheterization is the confirmatory test of choice for the diagnosis of pulmonary hypertension as well as the specific subgroup, in this case pulmonary arterial hypertension (PAH). Diagnosis is made when the mean pulmonary artery pressure is ≥ 20 mm Hg at rest and there is no evidence of underlying pulmonary and left heart conditions (e.g., valvular heart disease, systolic dysfunction, diastolic dysfunction). While PAH is often idiopathic, amphetamine and cocaine use have been associated with development of PAH. This patient has evidence of right-sided heart failure from her PAH, resulting in cor pulmonale. This indicates a worse prognosis.

This patient has chronic thromboembolic pulmonary hypertension (CTEPH), which can manifest with cor pulmonale. CTEPH can result from single or recurrent episodes of pulmonary embolism and should be suspected when pulmonary hypertension (PH) is diagnosed, especially in patients with risk factors for venous thromboembolism (e.g., malignancy, recent surgery). Decreased vascular markings on chest x-ray (i.e., Westermark sign) and bruits over the lung fields (i.e., flow murmurs over obstructed lung vessels) indicate diffuse pulmonary hypoperfusion and are characteristic of CTEPH. V/Q scan should be performed to differentiate CTEPH from pulmonary arterial hypertension (PAH), the two most likely diagnoses in this setting. Although this patient directly underwent right heart catheterization, this study is usually performed along with pulmonary angiography to confirm the diagnosis. Treatment of CTEPH involves life-long anticoagulation and pulmonary thromboendarterectomy in suitable patients. The causes of pulmonary hypertension can be classified into five groups: (1) idiopathic or hereditary, (2) left-sided heart disease, (3) chronic hypoxic lung disease, (4) chronic thromboembolism, and (5) unclear multifactorial mechanisms (e.g., sarcoidosis, metabolic disease, chronic hemolytic anemia).

Premature ventricular contractions

Postoperative arrhythmia (e.g., PVCs) is a common finding following cardiac and noncardiac surgery. The underlying pathophysiology is often complex but contributing factors may include high levels of catecholamines (endogenously due to the perioperative stress state; exogenous in the case of cardiovascular support), electrolyte or acid-base imbalances (e.g., hypokalemia, hypomagnesemia), reduced ventilation (leading to hypoxia and/or hypercarbia), and certain drugs. This patient takes a thiazide diuretic (hydrochlorothiazide), which is associated with an increased risk of hypokalemia. In cardiac cells, hypokalemia inhibits cardiac Na-K ATPase and causes prolonged ventricular repolarization, which predisposes to arrhythmias. Most patients with PVCs are asymptomatic and treatment (e.g., with antiarrhythmics or catheter ablation) is only required if PVCs are frequent or significantly symptomatic.

PVCs are often asymptomatic but can manifest with a feeling of “skipped beats.” If PVCs are frequent, symptoms such as palpitations, lightheadedness, dizziness, and irregular heartbeat, can occur. The PVCs in this healthy young patient are most likely triggered by lack of sleep and stress due to studying. Other common triggers include caffeine, alcohol, or nicotine consumption. In patients with frequent or long episodes of PVCs, further diagnostic studies (e.g., echocardiography) are indicated to assess for underlying heart disease. Because this is the first incident of PVCs in this patient, no treatment is necessary at this time; however, observation and rest are recommended to monitor for and potentially reduce the frequency of episodes.

Rheumatic fever

Intramuscular benzathine penicillin every 4 weeks for 10 years (or until 21 years of age, whichever is longer) is recommended for secondary prophylaxis of recurrent acute rheumatic fever in patients with manifestations of carditis but no permanent valvular damage. Patients and their families should be educated on early recognition of symptoms of ARF and the importance of adhering to prophylaxis.

Acute rheumatic fever (ARF) is a complication of untreated group A streptococcal tonsillopharyngitis. Major manifestations of ARF include arthritis, Sydenham chorea, subcutaneous nodules, erythema marginatum, and cardiac valve disease, of which mitral valve involvement is most common. Valve disease occurs as a result of antibodies against bacterial M proteins cross-reacting with valvular self-antigens through a process known as molecular mimicry, which results in valvular destruction. The mechanism of Sydenham chorea is thought to be similar and result from antibody cross-reactivity with basal ganglia structures. In the majority of cases, Sydenham chorea is self-limiting, with most patients seeing an improvement within a few weeks and nearly all patients fully recovered by six months.

This patient's symptoms (dyspnea, jugular venous distension, bilateral ankle edema, S3 gallop) and chest x-ray findings (enlarged cardiac silhouette, prominent vascular markings) suggest acute heart failure most likely due to carditis. His well-demarcated, erythematous, ring-shaped macules and patches are consistent with erythema marginatum. In the context of his recently untreated sore throat (most likely due to a group A streptococcal infection), the presence of carditis and erythema marginatum (two of the major revised Jones criteria) is consistent with acute rheumatic fever.

Renin-angiotensin-aldosterone system inhibitors

Dry cough is a characteristic side effect of angiotensin-converting enzyme inhibitors (ACE inhibitors). ACE inhibitors decrease blood pressure by inhibiting the renin-angiotensin-aldosterone system (RAAS). Inhibition of ACE also causes an increase in bradykinin, which can lead to bronchoconstriction and dry cough. If cough caused by ACE inhibitors is present, discontinuation of ACE inhibitors and switching to angiotensin receptor blockers (ARB) such as candesartan is recommended. Cough is a rare adverse effect of ARBs, as these agents do not influence the breakdown of kinins. Other common adverse effects of ACE inhibitors include hypotension, hyperkalemia, a decrease in glomerular filtration rate, and angioedema.

ACE inhibitors such as enalapril have been found to decrease cardiac remodeling by slowing down the rate of left ventricular thinning and dilation after acute MI. This effect is achieved by decreasing preload and afterload due to blockage of angiotensin II. This patient's presentation with dyspnea on exertion, left ventricular dilation on echocardiogram, and worsening ejection fraction of 40% is consistent with mild to moderate HF. Indications for ACE inhibitors (and angiotensin II receptor antagonists) in the secondary prevention of MI include heart failure, left ventricular ejection fraction < 40%, hypertension, diabetes mellitus, stable chronic kidney disease, and ST-segment elevation MI (especially with anterior location). Beta blockers have also been shown to have anti-remodeling effects.

Renal artery stenosis

Unilateral kidney atrophy may result from reduced blood flow to a kidney, as seen with renal artery stenosis (RAS). Findings that are highly suggestive of RAS include treatment-resistant hypertension, a high plasma renin activity (PRA), and hypokalemia (due to activation of the renin-angiotensin-aldosterone system). This patient has a variety of risk factors (e.g. male sex, age ≥ 45 years, smoking history, dyslipidemia, peripheral artery disease) and clinical features (e.g. bilateral carotid bruits) of diffuse atherosclerotic disease, making RAS secondary to atherosclerotic disease most likely. A significant decline in renal function after initiation of ACE inhibitors or angiotensin receptor blockers is characteristic of RAS.

Supraventricular premature beats

Counseling to avoid potential triggers, such as caffeine and/or alcohol consumption, stress, and smoking, is indicated in otherwise healthy individuals with idiopathic APBs. Ruling out organic causes such as structural heart disease or electrolyte imbalances is required. In symptomatic cases (e.g., tachycardia or ventricular response), electrophysiological evaluation with concurrent ablation or medical therapy with beta blockers can be considered. In asymptomatic patients experiencing APBs without underlying structural heart defects, no treatment is required and reassurance that this condition is a harmless type of arrhythmia should be provided. In addition, this patient should be advised to avoid potential triggers of APBs, including caffeine, alcohol, and stress.

Supraventricular tachycardia

Vagal maneuvers are the initial step in the management of a stable patient with PSVT because they are quick, can be performed by the patient, and have no side effects. Common maneuvers are the Valsalva maneuver and carotid massage. The stimulated vagus nerve then acts on the sinoatrial and atrioventricular nodes, which slows the heart rate and reduces conduction velocity. Should vagal maneuvers fail, other options in the acute management phase include adenosine, beta blockers, and calcium channel blockers.

Alternative electrical conduction pathways (one fast and one slow) in the atrioventricular node (AV node) are the underlying cause of AVNRT. The presence of an extra, fast accessory pathway occasionally leads to a nonextinguishable circulating electrical impulse (reentrant circuit) within the AV node that activates the atria and ventricles simultaneously and at a rapid rate. This produces episodic symptoms of palpitations, dyspnea, chest pain, dizziness and/or syncope.

In a hemodynamically stable patient (i.e., no hypotension, altered mental status, chest pain, and/or signs of heart failure) with evidence of WPW syndrome, antiarrhythmics that slow conduction within the aberrant pathway and/or prolong the aberrant pathway's refractory period, such as procainamide, are used as a temporary measure. AV nodal blocking agents (e.g., adenosine, beta blockers, CCBs) should be avoided in patients with evidence of current ventricular preexcitation such as this patient's wide QRS complex because AV nodal blockage would result in increased conduction through the aberrant pathway, which could result in lifethreatening ventricular tachyarrhythmias. Definitive therapy of WPW syndrome, which is radioablation of the aberrant pathway, should be performed as early as possible.

If vagal maneuvers do not terminate AVNRT, IV adenosine administration is the next step in management. Adenosine has a rapid onset of action and successfully terminates AVNRT in over 80% of cases. During IV administration, patients should be in the supine position and undergo continuous blood pressure and electrocardiographic monitoring. Adenosine slows down conduction in the AV node, resulting in short-term heart block, which can create an uncomfortable sensation that patients should be made aware of beforehand. Adverse effects include facial flushing and shortness of breath, hypotension, and bradycardia. Patients with asthma and reactive airway disease should not be given adenosine because of the risk of bronchospasm.

An accessory atrioventricular pathway that connects the atria and ventricles and bypasses the AV node is the underlying cause of WPW syndrome, a type of atrioventricular reciprocating tachycardia. The accessory pathway results in preexcitation of the ventricles and intermittent tachycardia, which can then lead to palpitations, dizziness, chest pain, dyspnea, and/or syncopes. Preexcitation is discernible on ECG as a shortened PR interval, while the subsequent myocardial conduction leads to a "slurred" upstroke in the QRS complex called a delta wave. This delta wave is not present in all patients with WPW syndrome.

Sinus node dysfunction

Sick sinus syndrome (SSS) refers to sinus node dysfunction and is most commonly caused by age-related degeneration and fibrosis, leading to abnormal automaticity (generation of electrical impulse) and/or abnormal conduction. SSS may also be caused or exacerbated by medications, including beta blockers (e.g., metoprolol). Diagnosis can be challenging, as arrhythmias are often transient and not always captured on 12-lead ECG. If clinical suspicion is high and ECG is unrevealing, a Holter monitor or event monitor should be considered to confirm the diagnosis. This patient's symptoms of cerebral hypoperfusion (presyncope) and evidence of bradycardia with sinus pause are enough to confirm the diagnosis. Palpitations, dyspnea, and irregular tachycardia on examination suggest that he has tachycardia-bradycardia syndrome. Symptomatic SSS is an indication for pacemaker placement.

Shock

Acute myocardial infarction is the most likely diagnosis in this older patient who presents with features of cardiogenic shock. Myocardial infarction causes an acute reduction in cardiac function that usually affects the left ventricle (95% of patients). Loss of left ventricular function leads to an increase in left atrial pressure, which is measured as an increase in PCWP. Progressive loss of cardiac function further impedes venous return to the heart, leading to a high CVP. In addition, there is a decrease in cardiac output and cardiac index, which is countered by systemic vasoconstriction in an attempt to maintain central perfusion. This vasoconstriction leads to an increased SVR and cool extremities with delayed capillary refill. A filling defect of a pulmonary artery on CT pulmonary angiography indicates pulmonary embolism (PE). Massive PE can cause major obstruction of the pulmonary vasculature, resulting in increased right heart pressures and features of right heart failure, like jugular venous distension. Obstruction of the pulmonary vessels leads to a decreased right heart output, resulting in normal or mildly decreased PCWP and decreased left ventricular end-diastolic volume, which leads to decreased cardiac output and, consequently, obstructive shock. SVR increases to compensate for the decrease in cardiac output.

An increase in heart rate is the first compensatory mechanism for hypovolemic shock and may be seen as early as class I hemorrhagic shock. In this patient, blood loss has resulted in hypovolemia and decreased stroke volume. The heart rate increases (as a result of intracardiac and arterial baroreceptor reflexes) to help maintain cardiac output. Initially, this mechanism may be sufficient to compensate for volume loss; patients in class I hemorrhagic shock may be otherwise asymptomatic. As shock progresses, compensatory mechanisms become overwhelmed by volume loss, resulting in further derangements in vital signs (e.g., tachycardia, hypotension, tachypnea, hypoxemia) and damage to multiple organ systems.

This profile is suggestive of distributive shock, which is a collective term for shock that results in pathologic vasodilation, leading to decreased SVR. The most common etiology is septic shock (in this case likely due to urinary tract infection), but it can also be caused by neurogenic shock or anaphylactic shock. Circulating cytokines and bacterial toxins cause pathologic vasodilation and lead to decreased SVR (afterload), as well as decreased CVP and PCWP (preload). Consequently, there is an increase in heart rate aimed at increasing cardiac output. Patients with septic shock often have warm, flushed skin as a result of this pathophysiology. In the late stage of septic shock, there may be a decrease in cardiac output and therefore patients may present with cold, pale skin with a delayed capillary refill.

The most important initial steps in the management of septic shock are measurement of serum lactate, early administration of empiric antibiotic therapy after blood cultures have been obtained, aggressive fluid resuscitation with crystalloids, and additional vasopressor

therapy in patients who are refractory to intravenous fluid management (hour-1 bundle for sepsis).

Stroke

Hypertension is the strongest predisposing factor for both ischemic and hemorrhagic stroke. Ischemic stroke is primarily caused by large artery atherosclerosis (for which hypertension is a major risk factor), whereas hemorrhagic stroke is most often due to rupture of vessels that have been damaged by chronic arterial hypertension. The most significant nonmodifiable risk factor is age > 65 years. Other important predisposing factors for ischemic stroke include conditions that increase the thromboembolic risk such as diabetes mellitus, atrial fibrillation, and carotid artery stenosis. Risk factors for hemorrhagic stroke include conditions that lead to vascular damage, such as vasculitis, malignancy, and previous ischemic stroke. This patient's risk for hypertension-related stroke is further elevated because his blood pressure is not optimally controlled. According to current recommendations by the American Heart Association and American College of Cardiology, blood pressure should not exceed a maximum of < 130/80 mm Hg in patients with diabetes mellitus.

A right-to-left cardiac shunt (e.g., patent foramen ovale or atrial septal defect) allows paradoxical emboli originating from the venous system to pass directly from the right atrium into the left atrium, from which point they may enter the cerebral arterial system. In a young patient, stroke symptoms (e.g., unilateral weakness, hyperreflexia, facial droop) and signs of DVT should raise concern for paradoxical embolism. This patient should have an immediate stroke workup (e.g., noncontrast head CT, possible thrombolysis). Furthermore, ultrasonography should be performed to confirm DVT. Because paradoxical embolism is a diagnosis of exclusion, all other causes must be excluded after the patient has been stabilized. Given the risk of pulmonary embolism and recurrent cerebral emboli, this patient should be started on anticoagulant therapy once cerebral hemorrhage is ruled out. Suspected patent foramen ovale should be confirmed with echocardiography so that it can be surgically or percutaneously closed to prevent recurrent emboli.

Syphilis

In addition to tabes dorsalis and Argyll Robertson pupil, patients with tertiary syphilis are at risk of developing thoracic aortic aneurysm (TAA) from aortitis. Treponemal-mediated destruction of the vasa vasorum classically affects the ascending aorta and can also lead to aortic root dilatation and aortic regurgitation. These cardiovascular complications are late manifestations of syphilis, and typically only occur after 15 years of untreated infection.

Syncope

Syncope due to carotid sinus hypersensitivity is seen in patients with carotid sinus syndrome. Pressure on the carotid sinuses (e.g., during a massage, when shaving, tightening a necktie) results in vagal activation, which leads to bradycardia and decreased blood pressure. A decrease in blood pressure leads to decreased cerebral perfusion. No treatment is required other than to advise the patient to avoid triggering activities.

Transient ischemic attack

A patient with TIA and concomitant Afib on initial presentation should undergo evaluation for anticoagulation to prevent future complications of Afib (e.g., systemic embolization with TIA). In women with Afib and a CHA2DS2-VASc score ≥ 3 (and men with a score ≥ 2), oral anticoagulation with either warfarin or a direct oral anticoagulant (DOAC), e.g., rivaroxaban, is indicated. This patient's score is 6 (+1 for age 65–74 years, +1 for female sex category, +1 for history of hypertension, +2 for history of TIA, and +1 for history of diabetes mellitus). DOACs are preferred over warfarin in the long-term management of most patients with atrial fibrillation with an indication for anticoagulation. Exceptions include patients with rheumatic mitral stenosis, mechanical heart valve, and chronic severe kidney disease. Generally, patients with TIA should receive immediate antiplatelet therapy (e.g., aspirin) unless they have a clear indication for anticoagulation at initial presentation (e.g., Afib). If this is the case, antiplatelet therapy can be replaced with anticoagulation to prevent thromboembolism.

Transfusion reactions

Transfusion-associated circulatory overload (TACO) refers to volume overload that has developed secondary to the transfusion of blood products. It generally occurs within 12 hours of transfusion and is characterized by hypertension, wide pulse pressure, and evidence of volume overload (pulmonary edema, S3 gallop, jugular venous distention). Risk increases with the number of units transfused and can be minimized by increasing time intervals between transfusions and limiting the rate of intravenous administration. Treatment usually involves the use of supplemental oxygen and mobilization of fluid with diuresis.

Thromboangiitis obliterans

Smoking is the single most important risk factor for TAO. The exact mechanism by which smoking causes TAO is unknown, but direct endothelial cell toxicity from the components of tobacco is presumed to play a role. Complete cessation of smoking and other tobacco products is, therefore, the most important therapeutic measure to prevent gangrene and amputation.

Takotsubo cardiomyopathy

Takotsubo cardiomyopathy occurs as a result of a catecholamine surge following intense emotional stress or severe illness. The catecholamine surge leads to cardiotoxicity and subsequent reversible left ventricular dysfunction. Takotsubo cardiomyopathy and acute coronary syndrome (ACS) have similar manifestations, such as increased cardiac enzymes and signs of ischemia on ECG (e.g., ST-segment elevation), but coronary angiography shows no obstructive coronary artery disease in Takotsubo cardiomyopathy. Left ventricular wall motion abnormalities that extend beyond the vascular distribution of a single coronary artery are seen on echocardiography. Apical ballooning with a hypercontractile base is a characteristic finding but not seen in all patients. In hemodynamically stable patients, Takotsubo cardiomyopathy is generally treated as heart failure with reduced ejection fraction and therapy commonly involves ACE inhibitors and beta blockers. In hemodynamically unstable patients, vasopressor support may be required.

Trauma

Management of trauma patients follows the ABCDE approach. This patient's airway (A) and breathing (B) have been assessed and are stable (conscious patient with symmetric chest rise, lungs clear to auscultation). Although hemorrhage control has been achieved with the application of a tourniquet, this patient's vital signs (hypotension, tachycardia) indicate circulatory (C) failure. Immediate administration of intravenous fluids in order to restore and maintain adequate tissue perfusion is vital. The standard trauma protocol of establishing intravenous access via two large-bore lines is not possible; one intravenous line is not sufficient for large-volume fluid resuscitation in this patient with life-threatening hemorrhage. Therefore, establishing intraosseous access is the most appropriate next step in management. Then, disability (D) is assessed via evaluation of the patient's neurological status, and exposure (E) of the patient is performed to allow a thorough evaluation.

Patients in shock with a history of, or ongoing, severe hemorrhage should receive an initial bolus of intravenous saline followed by transfusion of type O Rh negative packed red blood cells (pRBCs). If available, fully crossmatched pRBCs are preferable for this purpose. Early resuscitation with blood reestablishes hemoglobin levels and, therefore, the oxygen-carrying capacity of the intravascular volume. The reestablished capacity prevents organ ischemia and associated metabolic acidosis, both of which can complicate shock. If hemorrhage is extensive and the patient continues to be hemodynamically unstable, plasma and platelets should be transfused in addition to pRBCs at a 1:1:1 ratio. Transfusion of these blood products counters the risk of developing coagulopathy, which is another complication of shock associated with acidosis, hypothermia, trauma itself, fibrinolysis, and dilution due to fluid transfusion. In addition to transfusion of pRBCs, management of this patient should include immediate transfer to the operating room for laparotomy.

Ventricular tachycardia

IV magnesium sulfate is the first-line treatment for TdP in hemodynamically stable patients. It is highly effective in terminating TdP as well as preventing recurrences, which is vital because patients are at an increased risk for ventricular fibrillation. Patients with a normal serum magnesium concentration also benefit from this intervention. TdP in this patient is most likely due to macrolide antibiotics, which are the first-line antibiotics for the treatment of community-acquired pneumonia. The macrolide antibiotic should be discontinued and treatment with doxycycline initiated.

Prompt pharmacologic cardioversion with intravenous antiarrhythmics such as procainamide, sotalol, or amiodarone is the first-line treatment for hemodynamically stable patients with sustained monomorphic VT. If pharmacologic treatment is unsuccessful or if the patient develops signs of hemodynamically unstable VT, electrical cardioversion should be performed. This patient has a history of myocardial infarctions and ischemic heart disease, which is the most common cause of VT.

Synchronized cardioversion is the treatment of choice for hemodynamically unstable cardiac arrhythmias such as atrial fibrillation, atrial flutter, and monomorphic VT with a palpable pulse. This patient has chest pain, a pulse of 192/min, and a blood pressure of 80/50 mm Hg, all of which indicate hemodynamic instability due to sustained monomorphic ventricular tachycardia. Therefore, synchronized cardioversion is the most appropriate next step in management.

A prolonged QT interval may be congenital or acquired, and typically remains asymptomatic until patients present with syncope or life-threatening arrhythmias such as TdP. Acquired prolongation of the QT interval can be caused by certain medications (e.g., amiodarone, methadone, ondansetron) or electrolyte imbalances (e.g., hypokalemia, hypomagnesemia, and hypocalcemia). This patient's history of ondansetron and methadone therapy makes drug-induced QT prolongation that progressed to TdP the most likely cause of his syncope. Treatment consists of administering magnesium sulfate regardless of baseline magnesium levels.

Valvular heart diseases

The patient underwent a porcine valve replacement for severe mitral valve regurgitation 12 years ago. Biological valves (both bovine and porcine) typically have a short lifespan due to sclerotic degeneration. If the prosthetic valve becomes dysfunctional, the patient may have to undergo open-heart surgery for valve replacement again. Possible complications of the biological prosthetic valve include obstruction/stenosis, as seen in this patient, and regurgitation, both of which may manifest with signs of CHF.

Biological prosthetic valves are preferred over mechanical prosthetic valves in patients > 65 years of age because the degeneration process is slower than in younger patients and they typically do not need further surgery to replace the valve again. In addition, anticoagulation is only needed for 3 months following the surgery. Thus, biologic prosthetic valves are also preferred in patients with a high risk of bleeding, and in women with a desire to have children, since certain anticoagulants (e.g., warfarin) are teratogenic.

Acquired tricuspid valve regurgitation and signs of right-sided heart failure in a previously healthy patient suggest a diagnosis of tricuspid valve endocarditis, for which intravenous drug use (IVDU) is the strongest predisposing factor. The most commonly isolated pathogens in infective endocarditis due to IVDU are Staphylococcus aureus (most common), streptococci, and enterococci.